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Supporting Information

Divergent and Stereoselective Synthesis of β-Silyl-α-Amino Acids through Palladium-Catalyzed Intermolecular Silylation of Unactivated Primary and Secondary C–H Bonds

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Supporting Information

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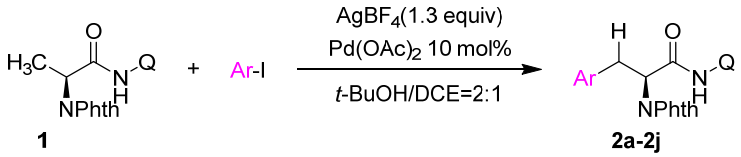
1. General Information

Toluene was dried by Sodium, distilled under reduced pressure and stored under nitrogen. $Pd(OAc)_2$ (Stream), Ag_2CO_3 (Adamas) were purchased from above mentioned company and used without additional purification. Other chemical reagents were commercially available and directly used without any further purification. NMR spectra were recorded on a Bruke Avance operating for ^1H NMR at 400 MHz, ^{13}C NMR at 100 MHz, and ^{19}F NMR at 376 MHz, using TMS as internal standard. The peaks were internally referenced to TMS (0.00 ppm) or residual undeuterated solvent signal (77.16 ppm for ^{13}C NMR). The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, m = multiplet, b = broad. Mass spectroscopy data of the products were collected on an HRMS-TOF instrumentor a low-resolution MS instrument using EI ionization and ESI ionization.

2. Experimental Section

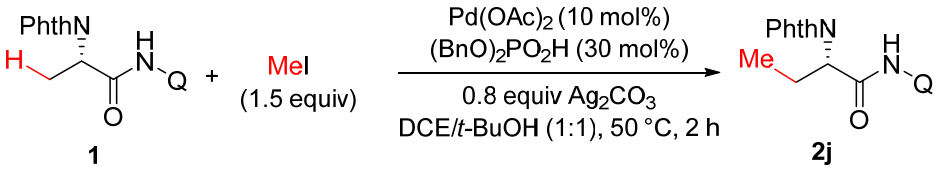
2.1 Praperation of Substrates

General Procedure for the Synthesis of 2a-2j via Pd-Catalyzed Monoarylation of Alanine Derivative 1[1]



To a 100-mL vial was added **1** (690.7 mg, 2.0 mmol), $Pd(OAc)_2$ (44.5 mg, 0.2 mmol), aryl iodide (2.4 mmol, for several specific reactions, 3.0 mmol of aryl iodide was used), $AgBF_4$ (506.2 mg, 2.6 mmol), and *t*-BuOH/DCE (10 mL + 5 mL). The mixture was stirred at 75 °C for 4 hours (for several specific substrates, the reactions were stirred for 24 hours). After cooling to room temperature, the reaction was diluted with dichloromethane (50 mL) and triethylamine (2 mL) was added to the mixture. After the mixture was maintained for 6 hours, it was then filtered through a pad of Celite and washed by dichloromethane (60 mL). The filtrate was washed by water (50 mL), and the aqueous phase was extracted with dichloromethane (2 × 30 mL). The combined organic phase was then washed by brine (50 mL), and dried over anhydrous MgSO4. Evaporation of organic solvent and purification by column chromatography gave the corresponding product **2a-2j**. **2a-2j** are known compounds.[1]

General Procedure for the Synthesis of 2k via Pd-Catalyzed Alkylation of Alanine Derivative 1[2]

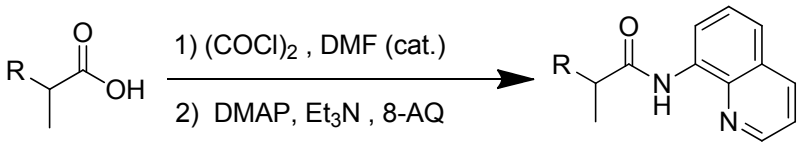


To a 30- mL resealable Schlenk flask was added *N*-phthaloyl-alanine 8-aminoquinoline amide (**1**) (0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), iodomethane (0.3 mmol), Ag_2CO_3 (0.16 mmol),

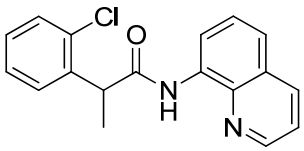
$(BnO)_2POOH$ (0.06 mmol), DCE/*t*-BuOH (1.5 mL, v/v = 1:1). The flask was then charged with N_2. The mixture was stirred at 50°C for 2 hours under N_2. After cooling to room temperature, the reaction was diluted with dichloromethane (5 mL) and then filtered through a pad of Celite and washed by dichloromethane (30 mL). Evaporation of organic solvent and purification by column chromatography gave the corresponding product **2k**. **2k** is known compound.[2]

General Procedure for synthesis of compound 5[3]

Compounds **5d, 5h, 5j** and **5t** were prepared from the corresponding carboxylic acids and 8-aminoquinoline (8-AQ). Other Compounds **(5a-5c, 5e-5g, 5i, 5k-5s, 5u and 5v)** are known compounds.[3]

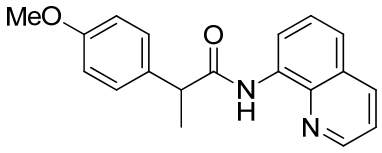


The corresponding carboxylic acid (10 mmol) was treated with (COCl)2 (12 mmol, 1.2 equiv) and DMF (0.1 mL) in DCM (30 mL) and stirred at room temperature overnight under N2. Then, the remained (COCl)2 and solvent were removed by evaporation. The residue acyl chloride was diluted with DCM (20 mL) for further use. To a stirring solution of 8-aminoquinoline (8-AQ, 10 mmol, 1.0 equiv), Et3N (12 mmol) and DMAP (1.0 mmol, 10 mol%) in DCM (30 mL) was added dropwise the solution of acyl chloride in DCM at 0-5°C under nitrogen atmosphere. After the addition, the resulting mixture was warmed to room temperature and stirred overnight. The reaction was quenched with water at 0 °C and diluted with DCM (30 mL). The resulting solution was washed sequentially by aqueous HCl (20 mL, 1.0 M), saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic phase was dried over anhydrous $MgSO_4$ and then evaporated under vacuum. The residue was purified by column chromatography to afford the aliphatic amide.



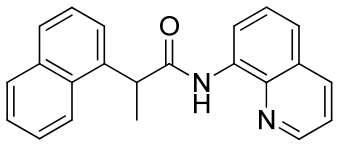
2-(2-chlorophenyl)-N-(quinolin-8-yl)propanamide 5d

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.00 (br, 1H), 8.75 (d, *J* = 7.2 Hz, 1H), 8.71 (d, *J* = 2.8 Hz, 1H), 8.08 (d, *J* = 8.0 Hz, 1H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.51-7.36 (m, 4H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.20 (t, *J* = 7.6 Hz, 1H), 4.48 (q, *J* = 6.8 Hz, 1H), 1.68 (d, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.89, 148.31, 138.69, 138.56, 136.26, 134.67, 133.89, 129.80, 128.69, 128.55, 127.95, 127.61, 127.39, 121.64, 121.62, 116.45, 44.49, 17.73.



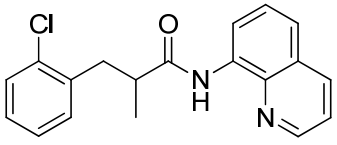
2-(4-methoxyphenyl)-N-(quinolin-8-yl)propanamide 5h

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.88 (br, 1H), 8.76 (d, *J* = 7.6 Hz, 1H), 8.70 (dd, *J* = 2.4, 1.2 Hz, 1H), 8.09 (d, *J* = 8.0 Hz, 1H), 7.52-7.37 (m, 5H), 6.91 (d, *J* = 7.6 Hz, 2H), 3.88 (q, *J* = 6.8, 1H), 3.79 (s, 3H), 1.66 (d, *J* = 7.2, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 173.19, 158.97, 148.22, 138.58, 136.33, 134.70, 133.37, 128.82, 127.97, 127.45, 121.59, 121.48, 116.34, 114.45, 77.48, 77.16, 76.84, 55.41, 47.91, 18.83.



2-(naphthalen-1-yl)-N-(quinolin-8-yl)propanamide 5j

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (br, 1H), 8.77 (d, *J* = 7.6 Hz, 1H), 8.50 (d, *J* = 3.6 Hz, 1H), 8.24 (d, *J* = 8.4 Hz, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 7.2 Hz, 1H), 7.57-7.46 (m, 4H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.28 (dd, *J* = 8.0, 4.0 Hz, 1H), 4.70 (dd, *J* = 13.6, 6.4 Hz, 1H), 1.86 (d, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.23, 148.14, 138.54, 137.03, 136.16, 134.67, 134.29, 131.80, 129.16, 128.22, 127.89, 127.39, 126.70, 125.91, 125.04, 123.44, 121.52, 121.48, 116.27, 45.04, 18.33.



3-(2-chlorophenyl)-2-methyl-N-(quinolin-8-yl)propanamide 5t

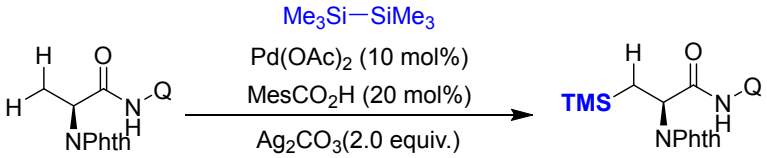
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (br, 1H), 8.79-8.75 (m, 2H), 8.12 (d, *J* = 8.0 Hz, 1H), 7.54-7.46 (m, 2H), 7.42 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.35 (m, 1H), 7.28 (dd, *J* = 5.4, 3.8 Hz, 1H), 7.10 (dd, *J* = 5.7, 3.5 Hz, 2H), 3.30 (dd, *J* = 12.9, 6.5 Hz, 1H), 2.99 (ddd, *J* = 29.1, 13.4, 7.1 Hz, 2H), 1.36 (d, *J* = 6.6 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$) δ 174.37, 148.23, 138.54, 137.45, 136.37, 134.63, 134.31, 131.75, 129.69, 127.99, 127.50, 126.87, 121.66, 121.52, 116.57, 42.78, 38.24, 17.72.

2.2 Optimized Reaction Conditions

2.2.1 Optimization of Conditions for the Synthesis of β-TMS-L-Ala via Pd(II)-Catalyzed Primary C-H Silylation

Table S1. Optimization of primary C-H silylation: screening of solvents

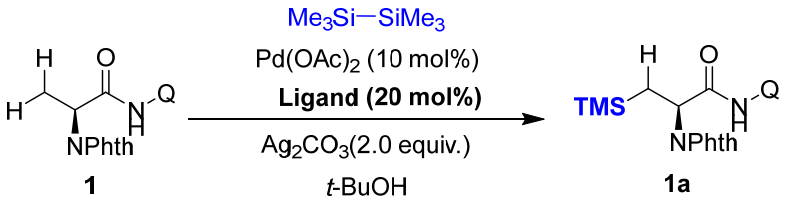


1 **1a**

Entry[a]	Solvent	Yield[b] of 1a/1
1	DCE	14%/78%
2	dioxane	12%/80%
3	toluene	41%/55%
4	*p*-xylene	44%/52%
5	PhCl	18%/76%
6	*t*-BuOH	63%/30%
7	*t*-AmylOH	61%/36%
8	DMF	trace
9	DMSO	ND.
10	THF	30%/63%

[a] The reactions were carried out with **1** (0.15 mmol), hexamethyldisilane (0.75 mmol), $Pd(OAc)_2$ (0.01 mmol), $MesCO_2H$ (0.02 mmol), Ag_2CO_3 (0.3 mmol), solvent (1.0 mL), air, 140 °C, 12 h. [b] Yield of ^1H NMR. ND = No detection.

Table S2. Optimization of primary C-H silylation: screening of ligands



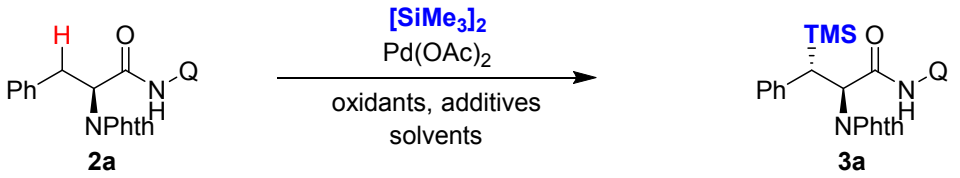
1 **1a**

Entry[a]	Ligand (20 mol%)	Yield[b] of 1a/1
1	$PivCO_2H$	60%/38%
2	$AdCO_2H$	63%/36%
3	TsOH	50%/47%
4	*N*-Boc-Ile-OH	76%/22%
5	*N*-Boc-Leu-OH	65%/30%
6	*N*-Boc-Val-OH	84%/15%
7	*N*-Boc-Gly-OH	80%/19%
8	*N*-Boc-Phala-OH	80%/15%
9	*N*-Ac-Val-OH	52%/46%
10	*N*-Ac-Ile-OH	51%/48%
11	*N*-Boc-PhGly-OH	75%/24%
12[b]	*N*-Boc-Val-OH	85%/13%

[a] The reactions were carried out with **1** (0.15 mmol), hexamethyldisilane (0.75 mmol), $Pd(OAc)_2$ (0.01 mmol), Acid (0.02 mmol), Ag_2CO_3 (0.3 mmol), *t*-BuOH (1.0 mL), air, 140 °C, 12 h. [b] Yield of ^1H NMR. [c] T= 125 °C.

2.2.2 Optimization of Conditions for the Synthesis of β-silyl-α-AAs via Pd(II)-Catalyzed Secondary C-H Silylation

Table S3. Optimization of the reaction conditions for secondary C-H silylation



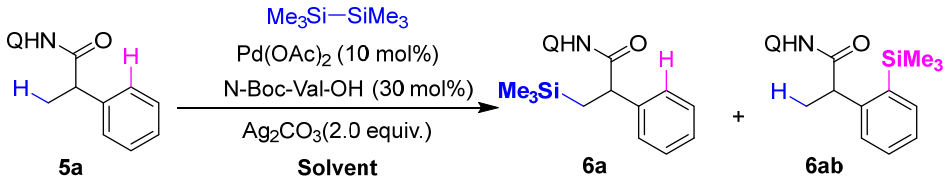
2a **3a**

Entry[a]	$Pd(OAc)_2$	Ag_2CO_3	Additives (x eq.)	Solvents	Yield[b] of 3a/2a	dr/3a[c]
1	standard reaction condition of primary C–H silylation				trace	---
2	0.10 eq.	2.0 eq.	---	1,4-dioxane	23%/68%	>20:1
3	0.10 eq.	2.0 eq.	---	*t*-BuOH	ND	---
4	0.10 eq.	2.0 eq.	$NaHCO_3$ (1.0)	1,4-dioxane	ND	---
5	0.10 eq.	2.0 eq.	$(BnO)_2PO_2H$ (0.2)	1,4-dioxane	trace	---
6	0.10 eq.	2.0 eq.	BQ (0.2)	1,4-dioxane	28%/59%	>20:1
7	0.10 eq.	2.0 eq.	2,6-diCl-BQ (0.2)	1,4-dioxane	34%/36%	>20:1
8	0.10 eq.	2.0 eq.	2,6-diOMe-BQ (0.2)	1,4-dioxane	32%/46%	>20:1
9	0.15 eq.	2.0 eq.	2,6-diOMe-BQ (0.3)	1,4-dioxane	45%/35%	>20:1
10	0.15 eq.	2.0 eq.	2,6-diOMe-BQ (1.5)	1,4-dioxane	60%/22%	>20:1
11	0.15 eq.	0.5 eq.	2,6-diOMe-BQ (1.5)	1,4-dioxane	71%/11%	>20:1

[a] The reactions were carried out with **2a** (0.1 mmol), hexamethyldisilane (0.5 mmol), $Pd(OAc)_2$ (0.015 mmol), air, 125 °C, 12 h; [b] Yield of ^1H NMR; [c] Determined by ^1H NMR.

2.2.3 Optimization of Conditions for Pd(II)-Catalyzed Silylation of Primary C-H Bonds of Simple Aliphatic Propionic Acid Derivatives.

Table S4. Screening of solvents

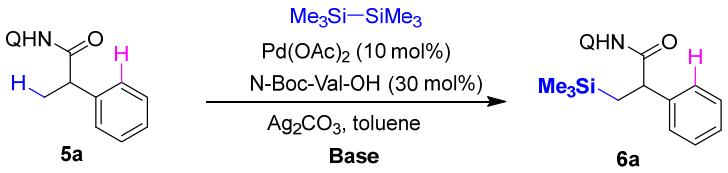


5a **6a** **6ab**

Entry[a]	Solvent	Yield[b] of 6a/5a/6ab
1	*t*-BuOH	5%/92%/ND
2	*t*-AmylOH	30%/53/ND
3	toluene	38%/55/ND
4	*p*-xylene	34%/52/ND
5	PhCl	12%/76/ND

[a] The reactions were carried out with **5a** (0.15 mmol), hexamethyldisilane (0.75 mmol), $Pd(OAc)_2$ (0.015 mmol), N-Boc-Val-OH (0.03 mmol), Ag_2CO_3 (0.3 mmol), solvent (1.0 mL), air, 140 °C, 12 h. [b] Yield of ^1H NMR. ND = No detection.

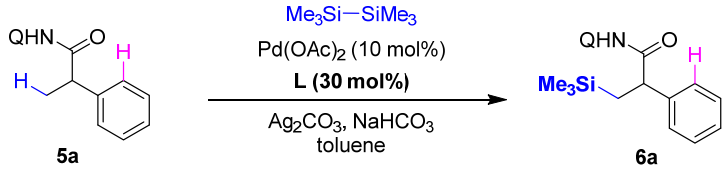
Table S5. Screening of bases



Entry[a]	Bases (2.0 eq.)	Yield[b] of 6a/5a
1	Li_2CO_3	39%/49%
2	Na_2CO_3	32%/60%
3	K_2CO_3	28%/37%
4	$NaHCO_3$	47%/44%
5	$KHCO_3$	35%/40%
6	LiOAc	31%/47%
7	NaOAc	28%/43%
8	KOAc	25%/36%
9	MesCOOK	44%/41%

[a] The reactions were carried out with **5a** (0.15 mmol), hexamethyldisilane (0.75 mmol), $Pd(OAc)_2$ (0.015 mmol), N-Boc-Val-OH (0.03 mmol), Ag_2CO_3 (0.3 mmol), $NaHCO_3$ (0.3 mmol), toluene (1.0 mL), air, 140 °C, 12 h. [b] Yield of ^1H NMR.

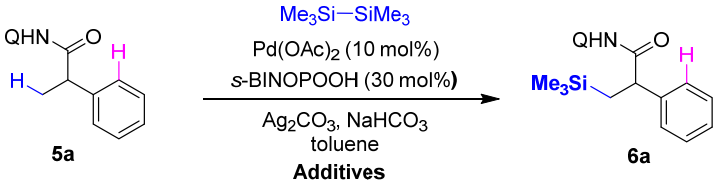
Table S6. Screening of ligands



Entry[a]	Ligands (0.3 eq.)	Yield[b] of 6a/5a
1	$AdCO_2H$	18%/73%
2	PivOH	20%/68%
3	$MesCO_2H$	25%/57%
4	Pyridine	5%/84%
5	*N*-Boc-Ile-OH	11%/76%
6	*N*-Boc-Gly-OH	32%/57%
7	*N*-Ac-Val-OH	36%/53%
8	BINAP	44%/47%
9	BINOL	8%/84%
10	*s*-BINOPOOH	61%/37%

[a] The reactions were carried out with **5a** (0.15 mmol), hexamethyldisilane (0.75 mmol), $Pd(OAc)_2$ (0.015 mmol), L (0.03 mmol), Ag_2CO_3 (0.3 mmol), $NaHCO_3$ (0.3 mmol), toluene (1.0 mL), air, 140 °C, 12 h. [b] Yield of ^1H NMR.

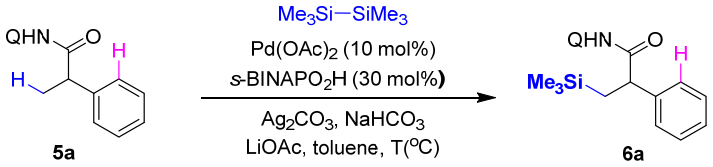
Table S7. Screening of additives



Entry[a]	Additives (2.0 eq.)	Yield[b] of 6a/5a
1	Li_2CO_3	58%/37%
2	Na_2CO_3	62%/32%
3	LiOAc	64%/34%
4	NaOAc	60%/34%
5	KOAc	28%/67%
6	LiTFA	3%/92%
7	KTFA	24%/57%
8	PivONa	7%/8%
9	$MesCO_2K$	11%/64%

[a] The reactions were carried out with **5a** (0.15 mmol), hexamethyldisilane (0.75 mmol), $Pd(OAc)_2$ (0.015 mmol), L (0.03 mmol), Ag_2CO_3 (0.3 mmol), $NaHCO_3$ (0.3 mmol), additives (0.3 mmol), toluene (1.0 mL), air, 140 °C, 12 h. [b] Yield of ^1H NMR.

Table S8. Screening of the equivalent of LiOAc

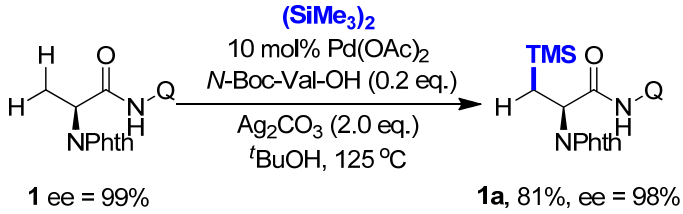


Entry[a]	LiOAc	T (°C)	Yield[b] of 6a/5a
1	2.0 eq.	135 °C	63%/34%
2	2.0 eq.	125 °C	64%/33%
3	2.0 eq.	115 °C	46%/43%
4	4.0 eq.	125 °C	52%/44%
5	3.0 eq.	125 °C	56%/40%
6	2.0 eq.	125 °C	63%/41%
7	1.0 eq.	125 °C	64%/44%
8	0.5 eq.	125 °C	65%/37%

[a] The reactions were carried out with **5a** (0.15 mmol), hexamethyldisilane (0.75 mmol), $Pd(OAc)_2$ (0.015 mmol), *s*-BINOPOOH (0.03 mmol), Ag_2CO_3 (0.3 mmol), $NaHCO_3$ (0.3 mmol), LiOAc (x mmol), toluene (1.0 mL), air, T °C, 12 h. [b] Yield of ^1H NMR.

2.3 General Procedures for Pd-Catalyzed C(sp^3)–H Silylation

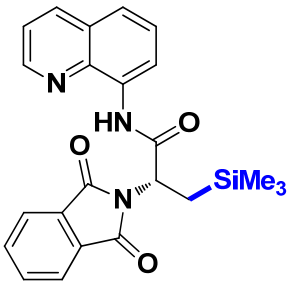
2.3.1 General Procedure for the synthesis of β-TMS-*L*-Ala via Pd-Catalyzed Silylation of Primary C–H Bonds (GP1)



1 ee = 99%

1a, 81%, ee = 98%

To an oven-dried 50 mL screw-capped vial was added substrate **1** (0.1 mmol), hexamethyldisilane (0. 5 mmol), $Pd(OAc)_2$ (2.3 mg, 0.01 mmol), *N*-Boc-*L*-Val-OH (0.02 mmol), Ag_2CO_3 (56 mg, 0.2 mmol), ^{t}BuOH (1.0 mL). The mixture was stirred for 12 h at 125 °C under air followed by cooling. The resulting mixture was filtered through a celite pad and concentrated in *vacuo*. The residue was purified by preparative TLC using hexane/EtOAc as the eluent to afford the product **1a.**



(*R*)-2-(1,3-dioxoisoindolin-2-yl)-N-(quinolin-8-yl)-3-(trimethylsilyl)propanamide 1a

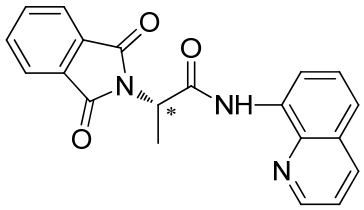
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.47 (br, 1H), 8.74-8.70 (m, 2H), 8.14 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.90 (dd, *J* = 5.2, 3.2 Hz, 2H), 7.75 (dd, *J* = 5.2, 3.2 Hz, 2H), 7.50 (d, *J* = 4.8 Hz, 2H), 7.42 (dd, *J* = 8.0, 4.0 Hz, 1H), 5.23 (dd, *J* = 12.0, 4.8 Hz, 1H), 2.08 (dd, *J* = 14.4, 12.0 Hz, 1H), 1.66 (dd, *J* = 14.4, 4.8 Hz, 1H), 0.05 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.41, 168.19, 148.50, 138.77, 136.40, 134.34, 134.21, 132.11, 128.03, 127.45, 123.73, 121.98, 121.73, 116.77, 52.41, 17.31, -1.31; **HRMS** (ESI-TOF) calcd for $C_{23}H_{23}ClN_3O_3Si$ (M^+): 417.1509, found: 417.1515; HPLC Chiralpack® AD-H column (n-hexane/isopropanol = 70:30, 1.0 mL/min) t_r = 8.794 min (major), t_r = 10.062 min (minor): 98% ee.

***DL*-/*L*-1** were prepared following the literature procedure.[1]

1: HPLC Chiralpack® AD-H column (n-hexane/isopropanol = 70:30, 1.0 mL/min) t_r = 14.327 min

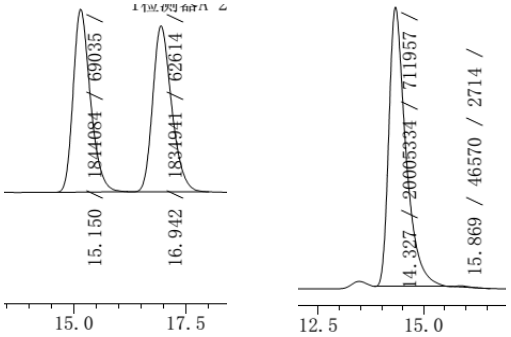
(major), t_r = 15.869 min (minor): 99% ee.

***DL*-/*L*-1**



Chiral stationary phase: Chiralpack® AD-H, n-hexane/isopropanol = 70:30, 1.0 mL/min

Signal: VWD1 A, Wavelength = 220 nm



Area% report for *DL*/*L*-1:

***DL*-1**			***L*-1**		
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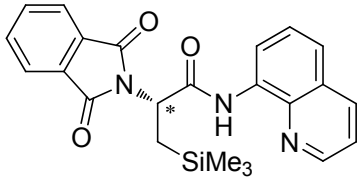
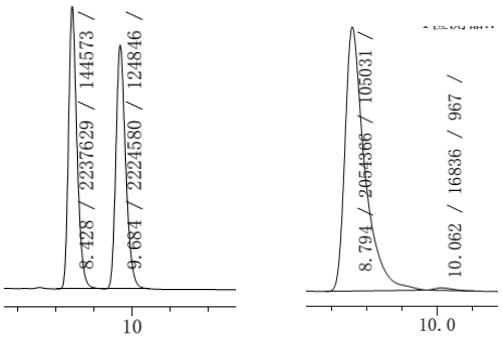
15.150	1844084	50.12	14.327	20005334	99.77
16.942	1834941	49.88	15.869	46570	0.23
Totals	3679025	100.00	Totals	20051903	100.00

***DL*-/*L*-1a**



Chiral stationary phase: Chiralpack® AD-H, n-hexane/isopropanol = 70:30, 1.0 mL/min

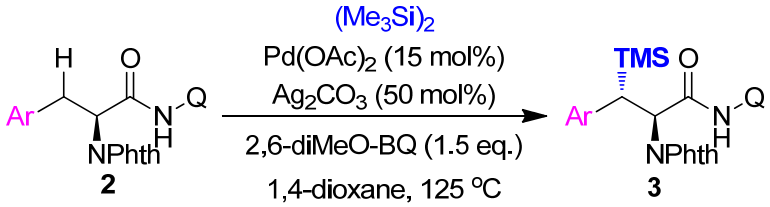
Signal: VWD1 A, Wavelength = 220 nm



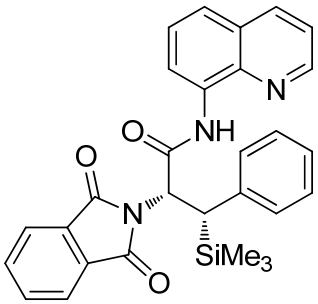
Area% report for *DL*/*L*-1a:

***DL*-1a**			***L*-1a**		
Retention Time (min)	Area (mAU*s)	Area %	Retention Time (min)	Area (mAU*s)	Area %
8.428	2237629	50.15	8.794	2054366	99.19
9.684	2224580	49.85	10.062	16836	0.81
Totals	4462209	100.00	Totals	2071202	100.00

2.3.2 General Procedure for the Synthesis of Chiral β-silyl-α-AAs via Pd-Catalyzed Silylation of Secondary C–H Bonds (GP2)



To an oven-dried 50 mL screw-capped vial was added substrate **2** (0.1 mmol), hexamethyldisilane (0. 5 mmol), $Pd(OAc)_2$ (3.5 mg, 0.015 mmol), Ag_2CO_3 (13.8 mg, 0.5 mmol), 2,6-diMeO-BQ (25.2 mg, 0.15 mmol), 1,4-dioxane (1.0 mL). The mixture was stirred for 12 h at 125 °C under air followed by cooling. The resulting mixture was filtered through a celite pad and concentrated in *vacuo*. The residue was purified by preparative TLC using hexane/EtOAc as the eluent to afford the product chiral β-silyl-α-amino acids **3.**



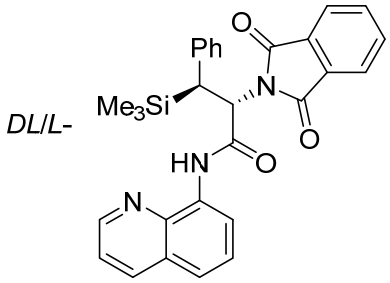
(2*R*,3*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-phenyl-*N*-(quinolin-8-yl)-3-(trimethylsilyl)propanamide 3a

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.93 (br, 1H), 8.93 (dd, *J* = 4.0, 1.6 Hz, 1H), 8.82-8.77 (m, 1H), 8.14 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.69 (m, 2H), 7.57 (td, *J* = 5.2, 2.0 Hz, 2H), 7.53 (d, *J* = 1.6 Hz, 1H), 7.52 (s, 1H), 7.46 (dd, *J* = 8.4, 4.0 Hz, 1H), 7.25-7.17 (m, 4H), 6.95 (ddd, *J* = 8.8, 5.2, 3.6 Hz, 1H), 5.60 (d, *J* = 13.6 Hz, 1H), 3.89 (d, *J* = 13.6 Hz, 1H), 0.02 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.26, 167.32, 148.81, 139.66, 138.98, 136.27, 134.61, 134.04, 131.37, 128.37, 128.07, 127.37, 125.54, 123.41, 122.26, 121.76, 117.46, 59.32, 36.53, -1.88; **HRMS** (ESI-TOF) calcd for $C_{29}H_{28}N_3O_3Si$ $(M+H)^+$: 494.1894, found: 494.1901; HPLC Chiralpack® AD-H column (n-hexane/isopropanol = 70:30, 1.0 mL/min) t_r = 13.317 min (minor), t_r = 10.062 min (major): 97% ee.

***L*-2a:** HPLC Chiralpak® AD-H column (n-hexane/isopropanol = 55:45, 0.90

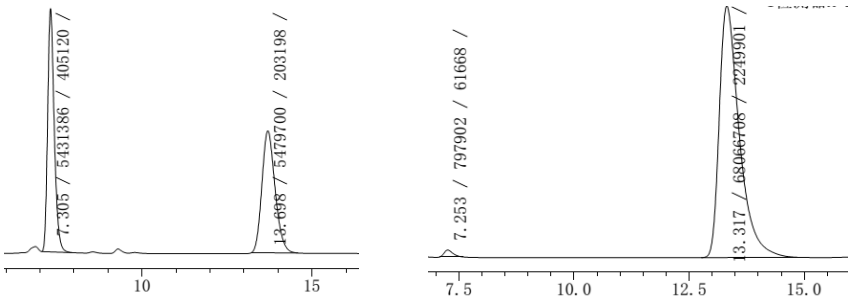
mL/min), t_r = 16.176 (minor), t_r = 24.049 (major), 98% ee.[1]

***DL*-/*L*-3a**



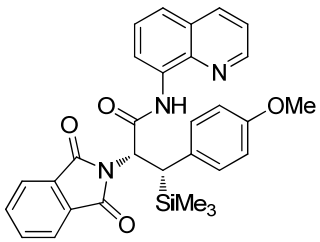
Chiral stationary phase: Chiralpack® AD-H, n-hexane/isopropanol = 70:30, 1.0 mL/min

Signal: VWD1 A, Wavelength = 220 nm



Area% report for *DL*/*L*-3a:

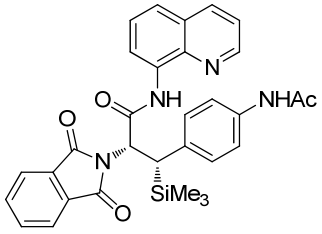
***DL*-3a**			***L*-3a**		
Retention Time (min)	Area (mAU*s)	Area %	Retention Time (min)	Area (mAU*s)	Area %
7.305	5431386	49.78	7.253	797902	1.16
13.698	5479700	50.22	13.317	68066708	98.84
Totals	10911086	100.00	Totals	68864611	100.00



(2*R*,3*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(4-methoxyphenyl)-*N*-(quinolin-8-yl)-3-(trimethylsilyl)propanamide 3b

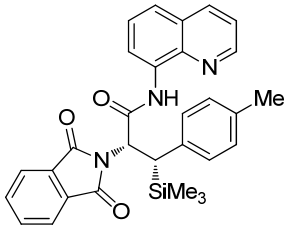
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.93 (br, 1H), 8.94 (d, *J* = 2.8 Hz, 1H), 8.80-8.78 (m, 1H), 8.15 (d, *J* = 7.2 Hz, 1H), 7.70 (dd, *J* = 5.2, 3.2 Hz, 2H), 7.58 (dd, *J* = 5.2, 3.2 Hz, 2H), 7.52 (d, *J* = 4.4 Hz, 2H), 7.46 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.02 (d, *J* = 8.4 Hz, 2H), 6.67 (d, *J* = 8.4 Hz, 2H), 5.53 (d, *J* =

13.6 Hz, 1H), 3.82 (d, *J* = 13.6 Hz, 1H), 3.66 (s, 3H), 0.01 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.32, 167.42, 157.41, 148.81, 139.00, 136.27, 134.64, 134.07, 131.53, 131.43, 128.08, 127.38, 123.46, 122.25, 121.76, 117.48, 113.85, 59.55, 55.18, 35.41, -1.88; **HRMS** (ESI-TOF) calcd for $C_{30}H_{30}N_3O4Si$ $(M+H)^+$: 524.2000, found: 524.2003.



(2*R*,3*S*)-3-(4-acetamidophenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)-3-(trimethylsilyl)propanamide 3c

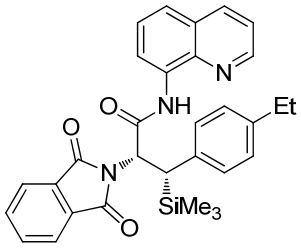
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.85 (br, 1H), 8.91 (dd, *J* = 4.02, 1. Hz, 1H),8.80- 8.75 (m, 1H), 8.15 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.75 (d, *J* = 8.4 Hz, 2H), 7.69 (dt, *J* = 7.2, 3.6 Hz, 2H), 7.58 (dd, *J* = 5.2, 3.2 Hz, 2H), 7.52 (d, *J* = 4.4 Hz, 2H), 7.46 (dd, *J* = 8.4, 4.0 Hz, 1H), 7.21 (d, *J* = 8.4 Hz, 2H), 5.63 (d, *J* = 13.6 Hz, 1H), 4.06 (d, *J* = 13.6 Hz, 1H), 2.47 (s, 3H), 0.03 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 197.88, 168.12, 166.77, 148.83, 146.16, 138.89, 136.31, 134.66, 134.41, 134.25, 131.20, 128.62, 128.05, 127.35, 123.58, 122.40, 121.82, 117.44, 58.52, 37.09, 26.54, -1.93; **HRMS** (ESI-TOF) calcd for $C_{31}H_{31}N_4O_4Si$ $(M+H)^+$: 551.2109, found: 551.2124.



(2*R*,3*S*)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)-3-(p-tolyl)-3-(trimethylsilyl)propanamide 3d

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.93 (br, 1H), 8.94 (dd, *J* = 4.0, 1.6 Hz, 1H), 8.79 (dd, *J* = 5.2, 3.6 Hz, 1H), 8.14 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.71-7.69 (m, 2H), 7.59-7.56 (m, 2H), 7.52-7.51 (m, 2H), 7.46 (dd, *J* = 8.4, 4.4 Hz, 1H), 6.99 (d, *J* = 8.4 Hz, 2H), 6.91 (d, *J* = 7.6 Hz, 2H), 5.57 (d, *J* = 13.6 Hz, 1H), 3.85 (d, *J* = 13.6 Hz, 1H), 2.14 (s, 3H), 0.01-0.00 (m, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.29, 167.44, 148.80, 138.98, 136.30, 136.26, 134.86, 134.63, 133.99, 131.45, 129.08, 128.06,

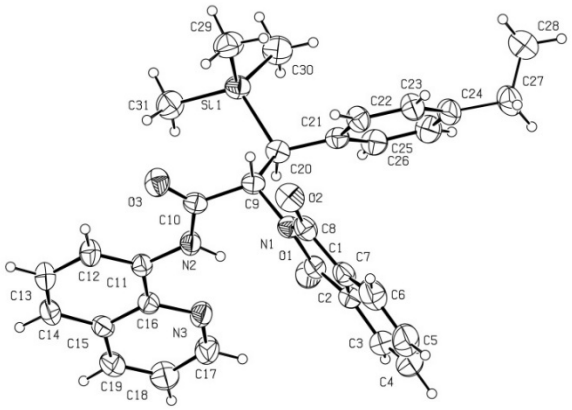
127.36, 123.43, 122.24, 121.75, 117.46, 59.48, 35.96, 20.99, -1.88; **HRMS** (ESI-TOF) calcd for $C_{30}H_{30}N_3O_3Si$ $(M+H)^+$: 508.2051, found: 508.2056.



(2*R*,3*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(4-ethylphenyl)-*N*-(quinolin-8-yl)-3-(trimethylsilyl)propanamide 3e

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.94 (br, 1H), 8.93 (dd, *J* = 4.0, 1.6 Hz, 1H), 8.80 (dd, *J* = 5.6, 3.2 Hz, 1H), 8.13 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.68 (dd, *J* = 5.6, 3.2 Hz, 2H), 7.56 (td, *J* = 5.2, 2.0 Hz, 2H), 7.52 (t, *J* = 2.4 Hz, 1H), 7.51 (s, 1H), 7.45 (dd, *J* = 8.4, 4.0 Hz, 1H), 7.00 (d, *J* = 8.4 Hz, 2H), 6.92 (d, *J* = 8.0 Hz, 2H), 5.57 (d, *J* = 13.6 Hz, 1H), 3.84 (d, *J* = 13.6 Hz, 1H), 2.43 (q, *J* = 7.6 Hz, 2H), 1.02 (t, *J* = 7.6 Hz, 3H), 0.01 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.33, 167.47, 148.80, 141.30, 138.99, 136.53, 136.25, 134.65, 133.95, 131.44, 128.06, 127.77, 127.36, 123.36, 122.22, 121.74, 117.46, 59.57, 36.04, 28.31, 15.43, -1.84; **HRMS** (ESI-TOF) calcd for $C_{31}H_{32}N_3O_3Si$ $(M+H)^+$: 522.2207, found: 522.2217.

X-ray Crystallographic Data of compound 3e



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Bond precision:  C-C = 0.0048 A          Wavelength=0.71073

Cell:            a=17.3625(12)     b=10.1657(5)     c=16.0229(10)
                 alpha=90          beta=90          gamma=90
Temperature:     293 K

                 Calculated                Reported
Volume           2828.1(3)                 2828.1(3)
Space group      P n a 21                  P n a 21
Hall group       P 2c -2n                  P 2c -2n
Moiety formula   C31 H31 N3 O3 Si          C31 H31 N3 O3 Si
Sum formula      C31 H31 N3 O3 Si          C31 H31 N3 O3 Si
Mr               521.68                    521.68
Dx,g cm-3        1.225                     1.225
Z                4                         4
Mu (mm-1)        0.119                     0.119
F000             1104.0                    1104.0
F000'            1104.75
h,k,lmax         20,12,19                  20,12,19
Nref             5191[ 2697]               5172
Tmin,Tmax        0.947,0.958               0.971,1.000
Tmin'            0.947

Correction method= # Reported T Limits: Tmin=0.971 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 1.92/1.00      Theta(max)= 25.350

R(reflections)= 0.0455( 3842)     wR2(reflections)= 0.1142( 5172)

S = 1.035                  Npar= 355
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Click on the hyperlinks for more details of the test.
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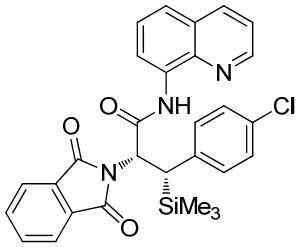
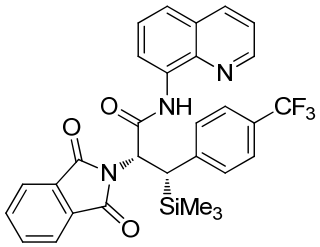


(2*R*,3*S*)-3-(4-chlorophenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)-3-(trimethylsilyl)propanamide 3f

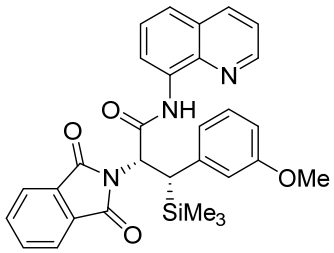
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.86 (br, 1H), 8.92 (dd, *J* = 4.0, 1.0 Hz, 1H), 8.80-8.75 (m, 1H), 8.15 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.74-7.69 (m, 2H), 7.63-7.60 m, 2H), 7.53-7.52 (m, 2H), 7.46 (dd, *J*

= 8.4, 4.0 Hz, 1H), 7.11 (d, *J* = 8.4 Hz, 2H), 7.05 (d, *J* = 8.8 Hz, 2H), 5.55 (d, *J* = 13.6 Hz, 1H), 3.91 (d, *J* = 13.6 Hz, 1H), 0.01 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.22, 166.96, 148.83, 138.94, 138.44, 136.32, 134.49, 134.26, 131.30, 131.19, 128.60, 128.08, 127.38, 123.59, 122.36, 121.81, 117.47, 58.92, 35.99, -1.94; **HRMS** (ESI-TOF) calcd for $C_{29}H_{27}ClN_3O_3Si$ $(M+H)^+$: 528.1505, found: 528.1505.



(2*R*,3*S*)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)-3-(4-(trifluoromethyl)phenyl)-3-(trimethylsilyl)propanamide 3g

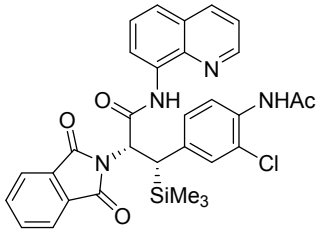
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.84 (br, 1H), 8.92 (dd, *J* = 4.0, 1.6 Hz, 1H), 8.79-8.77 (m, 1H), 8.15 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.71 (dd, *J* = 5.6, 3.2 Hz, 2H), 7.60 (dd, *J* = 5.6, 3.2 Hz, 2H), 7.53 (d, *J* = 4.4 Hz, 2H), 7.47 (dd, *J* = 8.4, 4.4 Hz, 1H), 7.40 (d, *J* = 8.2 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 5.62 (d, *J* = 13.6 Hz, 1H), 4.04 (d, *J* = 13.6 Hz, 1H), 0.03 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.20, 166.75, 148.85, 144.39, 138.91, 136.34, 134.41, 134.30, 131.21, 128.25, 127.76 (q, *J* = 32.2), 127.37, 125.37 (q, *J* = 3.8), 124.30 (q, *J* = 207.1), 123.60, 122.43, 121.84, 117.47, 58.60, 36.75, -1.94; **HRMS** (ESI-TOF) calcd for $C_{30}H_{27}F_3N_3O_3Si$ $(M+H)^+$: 562.1768, found: 562.1777.



(2*R*,3*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(3-methoxyphenyl)-*N*-(quinolin-8-yl)-3-(trimethylsilyl)propanamide 3h

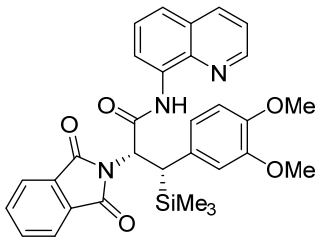
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.93 (br, 1H), 8.93 (dd, *J* = 4.0, 1.6 Hz, 1H), 8.79 (dd, *J* = 5.2, 4.0 Hz, 1H), 8.14 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.70 (dd, *J* = 5.6, 3.2 Hz, 2H), 7.58 (dd, *J* = 5.6, 3.2 Hz, 2H), 7.52 (d, *J* = 1.6 Hz, 1H), 7.51 (s, 1H), 7.46 (dd, *J* = 8.4, 4.4 Hz, 1H), 7.02 (t, *J* = 8.0 Hz, 1H), 6.70 (d, *J* = 7.6 Hz, 1H), 6.66-6.65 (m, 1H), 6.51 (dd, *J* = 8.0, 2.0 Hz, 1H), 5.59 (d, *J* = 13.6 Hz, 1H), 3.87 (d, *J* = 13.6 Hz, 1H), 3.71 (s, 3H), 0.03 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.27,

167.28, 159.48, 148.81, 141.27, 138.98, 136.27, 134.61, 134.08, 131.42, 129.31, 128.07, 127.36, 123.45, 122.28, 121.76, 117.48, 111.80, 59.32, 55.25, 36.66, -1.82; **HRMS** (ESI-TOF) calcd for $C_{30}H_{30}N_3O_4Si$ $(M+H)^+$: 524.2000, found: 524.2000.



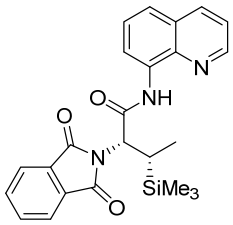
(2*R*,3*S*)-3-(4-acetamido-3-chlorophenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)-3-(trimethylsilyl)propanamide 3i

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.84 (br, 1H), 8.92 (dd, *J* = 4.0, 1.6 Hz, 1H), 8.79-8.74 (m, 1H), 8.18-8.13 (m, 2H), 7.73 (dd, *J* = 5.6, 3.2 Hz, 2H), 7.60 (dd, *J* = 5.6, 3.2 Hz, 2H), 7.52 (s, 1H), 7.51 (d, *J* = 1.2 Hz, 1H), 7.46 (dd, *J* = 8.4, 4.0 Hz, 2H), 7.15 (d, *J* = 2.0 Hz, 1H), 7.02 (dd, *J* = 8.8, 2.0 Hz, 1H), 5.53 (d, *J* = 13.6 Hz, 1H), 3.89 (d, *J* = 13.6 Hz, 1H), 2.14 (s, 3H), 0.02 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.14, 166.84, 148.84, 138.92, 136.66, 136.30, 134.45, 134.22, 132.28, 131.33, 128.06, 127.35, 123.66, 122.37, 122.23, 121.82, 121.28, 117.46, 58.80, 35.80, 24.94, -1.91; **HRMS** (ESI-TOF) calcd for $C_{31}H_{30}ClN_4O_4Si$ $(M+H)^+$: 585.1719, found: 585.1725.

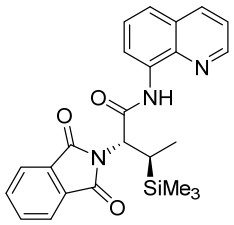


(2*R*,3*S*)-3-(3,4-dimethoxyphenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)-3-(trimethylsilyl)propanamide 3j

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.95 (br, 1H), 8.94 (dd, *J* = 4.0, 1.6 Hz, 1H), 8.79 (dd, *J* = 4.8, 4.0 Hz, 1H), 8.15 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.70 (dd, *J* = 5.6, 3.2 Hz, 2H), 7.59 (dd, *J* = 5.6, 3.2 Hz, 2H), 7.53 (d, *J* = 1.2 Hz, 1H), 7.52 (s, 1H), 7.46 (dd, *J* = 8.0, 4.4 Hz, 1H), 6.65-6.61 (m, 3H), 5.54 (d, *J* = 13.5 Hz, 1H), 3.81-3.78 (m, 4H), 3.72 (s, 3H), 0.03 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.36, 167.35, 148.81, 148.54, 146.72, 139.00, 136.29, 134.64, 134.16, 132.04, 131.40, 128.09, 127.37, 123.47, 122.28, 121.75, 117.53, 111.15, 59.50, 55.90, 55.75, 35.90, -1.82; **HRMS** (ESI-TOF) calcd for $C_{31}H_{32}N_3O_5Si$ $(M+H)^+$: 554.2106, found: 554.2108.



5k

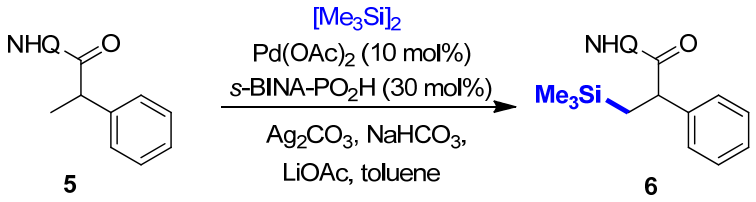


5k'

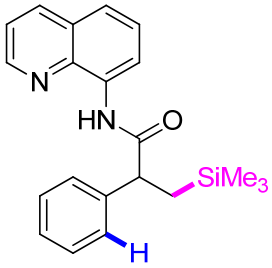
2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)-3-(trimethylsilyl)butanamide 5k and 5k'

3k:3k' = 3:1; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.75 (br, 0.75 H), 10.72 (br, 0.25 H), 8.92 (dd, *J* = 4.0, 1.6 Hz, 0.25 H), 8.88 (dd, *J* = 4.4, 1.6 Hz, 0.75H), 8.78-8.72 (m, 1H), 8.14 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.91-7.86 (m, 2H), 7.75-7.70 (m, 2H), 7.53-7.48 (m, 2H), 7.44 (dd, *J* = 8.4, 4.0 Hz, 1H), 5.00 (d, *J* = 12.0 Hz, 0.75H), 4.96 (d, *J* = 12.0 Hz, 0.25H), 2.63-2.56 (m, 0.25H), 2.44-2.35 (m, 0.75H), 1.19 (d, *J* = 7.2 Hz, 0.75H), 0.99 (d, *J* = 7.6 Hz, 2.25H), 0.08 (s, 6.75H), -0.02 (s, 2.25H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.53, 168.26, 167.67, 167.47, 148.72, 139.00, 138.94, 136.28, 134.56, 134.52, 134.42, 134.37, 131.89, 131.72, 128.07, 127.40, 127.36, 123.80, 123.76, 122.09, 122.06, 121.74, 117.27, 117.16, 60.67, 60.08, 20.02, 19.67, 13.17, 12.60, -2.46; **HRMS** (ESI-TOF) calcd for $C_{24}H_{26}ClN_3O_3Si$ $(M+H)^+$: 432.1738, found: 432.1743.

2.3.3 General Procedure for the Synthesis of β-Silyl-Proponic Acids via Pd-Catalyzed Silylation of Primary C–H Bonds (GP3)

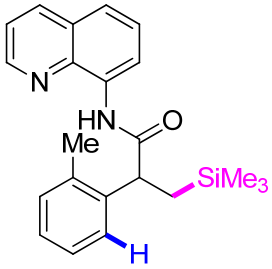


To an oven-dried 50 mL screw-capped vial was added substrate **5** (0.15 mmol), hexamethyldisilane (0.75 mmol), $Pd(OAc)_2$ (3.5 mg, 0.015 mmol), *s*-BINA-PO_2H (15.2 mg, 0.045 mmol), Ag_2CO_3 (82.8 mg, 0.3 mmol), $NaHCO_3$ (25.2 mg, 0.3 mmol), LiOAc (4.7 mg, 0.075 mmol), toluene (1.0 mL). The mixture was stirred for 10 h at 125 °C under air followed by cooling. The resulting mixture was filtered through a celite pad and concentrated in *vacuo*. The residue was purified by preparative TLC using hexane/EtOAc as the eluent to afford the product **6.**



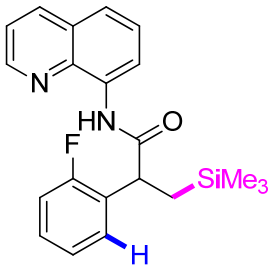
2-phenyl-*N*-(quinolin-8-yl)-3-(trimethylsilyl)propanamide 6a

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.93 (s, 1H), 8.75-8.73 (m, 2H), 8.08 (d, *J* = 8.0 Hz, 1H), 7.51-7.33 (m, 7H), 7.27-7.24 (m, 1H), 3.83 (t, *J* = 8.0, 1H), 1.62 (dd, *J* = 14.4, 6.4 Hz, 1H), 1.35 (dd, *J* = 14.8, 9.2 Hz, 1H), -0.07 (d, *J* = 0.8 Hz, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.22, 148.24, 141.71, 138.61, 136.34, 134.73, 128.94, 128.11, 127.98, 127.47, 127.40, 121.60, 121.45, 116.37, 51.00, 21.26, -1.15; **HRMS** (EI-TOF) calcd for $C_{21}H_{24}N_2OSi$ (M^+): 348.1658, found: 348.1656.



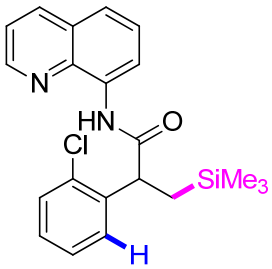
***N*-(quinolin-8-yl)-2-(o-tolyl)-3-(trimethylsilyl)propanamide 6b**

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.88 (br, 1H), 8.73 (d, *J* = 7.6 Hz, 1H), 8.68 (d, *J* = 4.0 Hz, 1H), 8.08 (d, *J* = 8.4 Hz, 1H), 7.55-7.42 (m, 3H), 7.37 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.25-7.15 (m, 3H), 4.09 (dd, *J* = 8.4, 7.2 Hz, 1H), 2.53 (s, 3H), 1.67 (dd, *J* = 14.8, 6.8 Hz, 1H), 1.33 (dd, *J* = 14.8, 8.8 Hz, 1H), -0.05 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.31, 148.25, 139.78, 138.62, 136.27, 135.77, 134.82, 130.94, 127.96, 127.70, 127.48, 127.19, 126.80, 121.58, 121.35, 116.24, 46.38, 20.62, 20.22, -1.03; **HRMS** (EI-TOF) calcd for $C_{22}H_{26}N_2OSi$ (M^+): 362.1814, found: 362.1816.



2-(2-fluorophenyl)-*N*-(quinolin-8-yl)-3-(trimethylsilyl)propanamide 6c

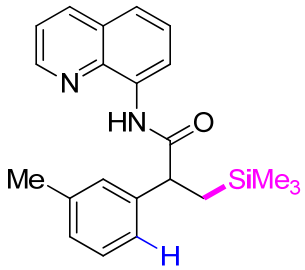
^{1}H NMR (400 MHz, $CDCl_3$) δδ 10.04 (br, 1H), 8.76 (m, 2H), 8.11 (d, *J* = 8.0 Hz, 1H), 7.58 (t, *J* = 7.2 Hz, 1H), 7.51-7.45 (m, 2H), 7.41 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.24-7.13 (m, 2H), 7.07 (t, *J* = 8.8 Hz, 1H), 4.24 (dd, *J* = 8.4, 7.2 Hz, 1H), 1.63 (dd, *J* = 14.4, 6.8 Hz, 1H), 1.34 (dd, *J* = 14.4, 8.8 Hz, 1H), -0.05 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.31, 160.38 (d, *J* = 243.1 Hz), 148.38, 138.65, 136.31, 134.75, 129.45 (d, *J* = 3.7 Hz), 128.81 (d, *J* = 8.3 Hz), 128.65 (d, *J* = 14.5 Hz), 128.00, 127.46, 124.74 (d, *J* = 3.4 Hz), 121.67, 121.57, 116.49, 115.60 (d, *J* = 22.6 Hz), 42.14 (d, *J* = 2.4 Hz), 42.13, 20.14, -1.23; ^{19}F NMR (376 MHz, $CDCl_3$) δ -118.26; **HRMS** (EI-TOF) calcd for $C_{21}H_{23}FN_2OSi$ (M^+): 366.1564, found: 366.1557.



2-(2-chlorophenyl)-*N*-(quinolin-8-yl)-3-(trimethylsilyl)propanamide 6d

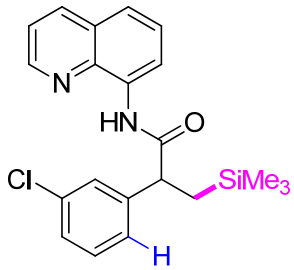
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.07 (br, 1H), 8.77 (d, *J* = 4.0 Hz, 1H), 8.73 (d, *J* = 7.2 Hz, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.51-7.38 (m, 4H), 7.27 (t, *J* = 7.6 Hz, 1H), 7.17 (t, *J* = 7.6 Hz, 1H), 4.48 (t, *J* = 7.6 Hz, 1H), 1.62 (dd, *J* = 14.8, 7.2 Hz, 2H), 1.33 (dd, *J* = 14.8, 8.4 Hz, 1H), -0.04 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.21, 148.39, 139.31, 138.62, 136.28,

134.83, 133.52, 129.69, 129.29, 128.43, 127.99, 127.54, 127.44, 121.67, 121.57, 116.48, 45.75, 20.66, -1.12; **HRMS** (EI-TOF) calcd for $C_{21}H_{23}ClN_2OSi$ (M^+): 382.1268, found: 382.1273.



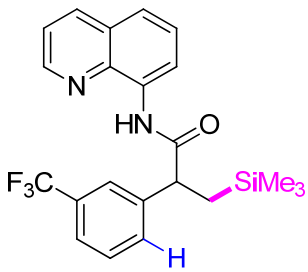
***N*-(quinolin-8-yl)-2-(m-tolyl)-3-(trimethylsilyl)propanamide 6e**

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.87 (br, 1H), 8.73 (d, *J* = 7.6 Hz, 1H), 8.68 (d, *J* = 4.0 Hz, 1H), 8.08 (d, *J* = 8.4 Hz, 1H), 7.55-7.42 (m, 3H), 7.37 (dd, *J* = 8.4, 4.4 Hz, 1H), 7.25-7.16 (m, 3H), 4.09 (t, *J* = 8.0 Hz, 1H), 2.53 (s, 3H), 1.67 (dd, *J* = 14.8, 6.8 Hz, 1H), 1.33 (dd, *J* = 14.8, 8.8 Hz, 1H), -0.05 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δδ 173.32, 148.26, 139.78, 138.62, 136.28, 135.77, 134.82, 130.94, 127.96, 127.70, 127.48, 127.19, 126.80, 121.58, 121.36, 116.24, 46.38, 20.62, 20.22, -1.03; **HRMS** (EI-TOF) calcd for $C_{22}H_{26}N_2OSi$ (M^+): 362.1814, found: 362.1816.



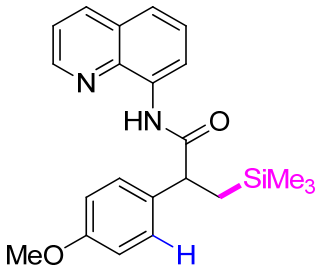
2-(3-chlorophenyl)-*N*-(quinolin-8-yl)-3-(trimethylsilyl)propanamide 6f

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.95 (br, 1H), 8.78 (d, *J* = 4.0 Hz, 1H), 8.73 (d, *J* = 7.2 Hz, 1H), 8.12 (d, *J* = 8.4 Hz, 1H), 7.52-7.39 (m, 6H), 7.30-7.23 (m, 2H), 3.79 (t, *J* = 8.0 Hz, 1H), 1.62 (dd, *J* = 14.4, 7.2 Hz, 1H), 1.30 (dd, *J* = 14.6, 8.5 Hz, 1H), -0.05 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.37, 148.37, 143.87, 138.60, 136.44, 134.73, 134.53, 130.15, 128.21, 128.02, 127.59, 127.50, 126.30, 121.72, 121.68, 116.50, 50.70, 21.49, -1.13; **HRMS** (EI-TOF) calcd for $C_{21}H_{23}ClN_2OSi$ (M^+): 382.1268, found: 382.1262.



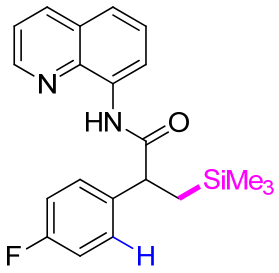
***N*-(quinolin-8-yl)-2-(3-(trifluoromethyl)phenyl)-3-(trimethylsilyl)propanamide 6g**

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.98 (br, 1H), 8.77 (d, *J* = 2.8 Hz, 1H), 8.72 (d, *J* = 6.0 Hz, 1H), 8.13 (d, *J* = 8.4 Hz, 1H), 7.79 (s, 1H), 7.72 (d, *J* = 7.2 Hz, 1H), 7.54-7.42 (m, 5H), 3.89 (t, *J* = 8.0 Hz, 1H), 1.66 (dd, *J* = 14.8, 7.2 Hz, 1H), 1.34 (dd, *J* = 14.7, 8.4 Hz, 1H), -0.05 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δδ 172.24, 148.38, 142.82, 138.61, 136.44, 134.46, 131.56, 131.22 (q, *J* = 32.0 Hz), 129.39, 128.02, 127.48, 124.90 (q, *J* = 3.8 Hz), 124.29 (q, *J* = 3.7 Hz), 124.26 (q, *J* = 270.7 Hz), 121.77, 116.52, 50.85, 21.68, -1.16; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.52; **HRMS** (EI-TOF) calcd for $C_{22}H_{23}F_3N_2OSi$ (M^+): 416.1532, found: 416.1533.



2-(4-methoxyphenyl)-*N*-(quinolin-8-yl)-3-(trimethylsilyl)propanamide 6h

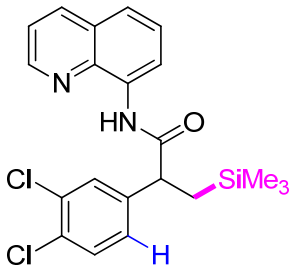
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.91 (br, 1H), 8.74 (d, *J* = 7.2 Hz, 2H), 8.11 (d, *J* = 8.4 Hz, 1H), 7.51-7.40 (m, 5H), 6.89 (d, *J* = 8.0 Hz, 2H), 3.79-3.75 (m, 4H), 1.58 (dd, *J* = 14.4, 6.4 Hz, 2H), 1.33 (dd, *J* = 14.4, 9.6 Hz, 1H), -0.07 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.65, 159.00, 148.26, 138.66, 136.37, 134.82, 133.77, 129.12, 128.01, 127.52, 121.61, 121.40, 116.35, 114.34, 55.42, 50.15, 21.25, -1.10; **HRMS** (EI-TOF) calcd for $C_{22}H_{26}N_2O_2Si$ (M^+): 378.1764, found: 378.1761.



2-(4-fluorophenyl)-*N*-(quinolin-8-yl)-3-(trimethylsilyl)propanamide 6i

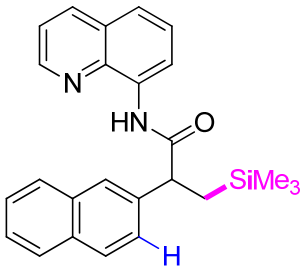
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.92 (br, 1H), 8.76-8.72 (m, 2H), 8.11 (d, *J* = 7.6 Hz, 1H), 7.52-7.45 (m, 4H), 7.41 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.04 (t, *J* = 8.4 Hz, 2H), 3.81 (dd, *J* = 8.4, 6.8 Hz, 1H), 1.60 (dd, *J* = 14.8, 6.8 Hz, 1H), 1.32 (dd, *J* = 14.8, 8.8 Hz, 1H), -0.07 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.05, 162.25 (d, *J* = 244.0 Hz), 148.32, 138.61, 137.49 (d, *J* = 3.1 Hz), 136.42, 134.62,

129.61 (d, J = 8.0 Hz,), 128.02, 127.49, 121.64 (d, J = 8.6 Hz,), 116.42, 115.86, 115.64, 50.22, 21.54, -1.13; **HRMS** (EI-TOF) calcd for $C_{21}H_{23}FN_2OSi$ (M^+): 366.1564, found: 366.1566.



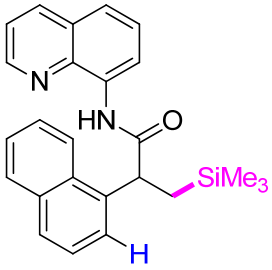
2-(3,4-dichlorophenyl)-*N*-(quinolin-8-yl)-3-(trimethylsilyl)propanamide 6l

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.96 (br, 1H), 8.79 (dd, J = 4.0, 1.2 Hz, 1H), 8.71 (dd, J = 6.8, 2.0 Hz, 1H), 8.13 (dd, J = 8.4, 1.2 Hz, 1H), 7.63 (d, J = 1.6 Hz, 1H), 7.53-7.35 (m, 5H), 3.78 (t, J = 8.0 Hz, 1H), 1.61 (dd, J = 14.8, 7.6 Hz, 1H), 1.27 (dd, J = 14.8, 8.0 Hz, 1H), -0.03 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.94, 148.42, 142.18, 138.56, 136.47, 134.37, 132.86, 131.40, 130.76, 129.96, 128.02, 127.47, 127.41, 121.83, 121.77, 116.55, 50.17, 21.62, -1.10; **HRMS** (EI-TOF) calcd for $C_{21}H_{22}Cl_2N_2OSi$ (M^+): 416.0878, found: 416.0876.



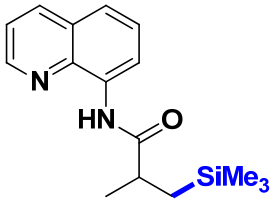
2-(naphthalen-2-yl)-*N*-(quinolin-8-yl)-3-(trimethylsilyl)propanamide 6k

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.00 (br, 1H), 8.74 (d, J = 7.6 Hz, 1H), 8.66 (d, J = 4.0 Hz, 1H), 8.08 (d, J = 8.4 Hz, 1H), 7.95 (s, 1H), 7.87-7.79 (m, 3H), 7.64 (d, J = 8.4 Hz, 1H), 7.51-7.42 (m, 4H), 7.37 (dd, J = 8.0, 4.0 Hz, 1H), 4.01 (t, J = 8.0 Hz, 1H), 1.72 (dd, J = 14.8, 7.2 Hz, 1H), 1.44 (dd, J = 14.8, 8.8 Hz, 1H), -0.06 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.08, 148.26, 139.30, 138.61, 136.34, 134.72, 133.75, 132.88, 128.76, 127.96, 127.80, 127.49, 126.83, 126.26, 126.12, 125.88, 121.61, 121.48, 116.37, 51.15, 21.22, -1.04; **HRMS** (EI-TOF) calcd for $C_{25}H_{26}N_2OSi$ (M^+): 398.1814, found: 398.1811.



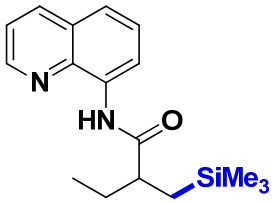
2-(naphthalen-1-yl)-*N*-(quinolin-8-yl)-3-(trimethylsilyl)propanamide 6j

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.93 (br, 1H), 8.74 (d, *J* = 7.6 Hz, 1H), 8.55 (dd, *J* = 4.0, 1.6 Hz, 1H), 8.31 (d, *J* = 8.4 Hz, 1H), 8.01 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.78 (dd, *J* = 12.4, 7.6 Hz, 2H), 7.59-7.37 (m, 5H), 7.29 (dd, *J* = 8.0, 4.0 Hz, 1H), 4.64 (t, *J* = 7.6 Hz, 1H), 1.82 (dd, *J* = 14.8, 7.2 Hz, 1H), 1.52 (dd, *J* = 14.8, 8.4 Hz, 1H), -0.06 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.29, 148.13, 138.54, 137.63, 136.16, 134.77, 134.40, 131.69, 129.19, 128.14, 127.89, 127.41, 126.61, 125.81, 125.77, 123.60, 121.50, 121.34, 116.17, 46.81, 20.75, -1.03; **HRMS** (EI-TOF) calcd for $C_{25}H_{26}N_2OSi$ (M^+): 398.1814, found: 398.1811.



2-methyl-*N*-(quinolin-8-yl)-3-(trimethylsilyl)propanamide 6m

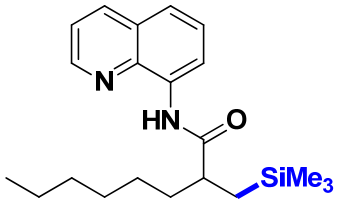
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.89 (br, 1H), 8.82-8.78 (m, 2H), 8.15 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.55-7.43 (m, 3H), 2.77-2.68 (m, 1H), 1.37 (d, *J* = 6.8 Hz, 3H), 1.20 (dd, *J* = 14.8, 6.8 Hz, 1H), 0.88 (dd, *J* = 14.8, 7.6 Hz, 1H), 0.06 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 176.41, 148.27, 138.65, 136.48, 134.81, 128.08, 127.61, 121.67, 121.37, 116.54, 39.37, 22.49, 21.45, -0.84; **HRMS** (EI-TOF) calcd for $C_{16}H_{22}N_2OSi$ (M^+): 286.1501, found: 286.1496.



***N*-(quinolin-8-yl)-2-((trimethylsilyl)methyl)butanamide 6n**

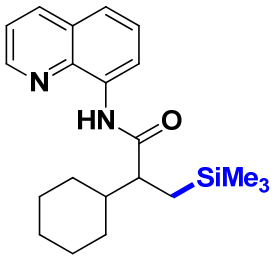
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.86 (br, 1H), 8.81 (d, *J* = 7.2 Hz, 2H), 8.16 (d, *J* = 8.0 Hz, 1H), 7.56-7.44 (m, 3H), 2.52-2.45 (m, 1H), 1.88-1.79 (m, 1H), 1.68-1.61 (m, 1H), 1.14 (dd, *J* = 14.8, 8.8

Hz, 1H), 0.99 (t, J = 7.2 Hz, 3H), 0.88 (dd, J = 14.8, 6.0 Hz, 1H), 0.03 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) 75.54, 148.31, 138.63, 136.47, 134.73, 128.10, 127.63, 121.68, 121.39, 116.59, 46.90, 29.68, 20.73, 12.19, -0.96; **HRMS** (EI-TOF) calcd for $C_{17}H_{24}N_2OSi$ (M^+): 300.1658, found: 300.1654.



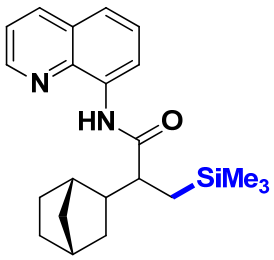
***N*-(quinolin-8-yl)-2-((trimethylsilyl)methyl)octanamide 6o**

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.85 (br, 1H), 8.83-8.79 (m, 2H), 8.16 (dd, J = 8.0, 1.2 Hz, 1H), 7.56-7.44 (m, 3H), 2.58-2.51 (m, 1H), 1.87-1.78 (m, 1H), 1.60-1.53 (m, 1H), 1.40-1.25 (m, 8H), 1.13 (dd, J = 14.8, 8.8 Hz, 1H), 0.91-0.82 (m, 4H), 0.03 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 175.71, 148.30, 138.63, 136.45, 134.75, 128.09, 127.63, 121.67, 121.36, 116.59, 45.31, 36.74, 31.85, 29.49, 27.69, 22.74, 21.11, 14.19, -0.94; **HRMS** (EI-TOF) calcd for $C_{21}H_{32}N_2OSi$ (M^+): 356.2284, found: 356.2285.



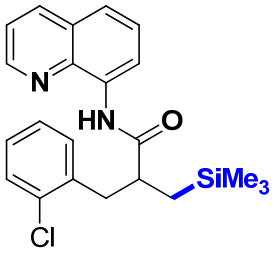
2-cyclohexyl-*N*-(quinolin-8-yl)-3-(trimethylsilyl)propanamide 6p

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.82 (br, 1H), 8.83-8.80 (m, 2H), 8.16 (d, J = 8.0 Hz, 1H), 7.55-7.44 (m, 3H), 2.33-2.27 (m, 1H), 1.97 (d, J = 12.4 Hz, 1H), 1.79 (t, J = 13.2 Hz, 2H), 1.71-1.58 (m, 3H), 1.28-0.90 (m, 7H), -0.01 (s, 9H).; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 174.81, 148.32, 138.62, 136.43, 134.66, 128.10, 127.65, 121.66, 121.33, 116.54, 51.31, 43.40, 30.96, 30.79, 26.64, 26.59, 26.55, 17.22, -1.14; **HRMS** (EI-TOF) calcd for $C_{21}H_{30}N_2OSi$ (M^+): 354.2127, found: 354.2131.



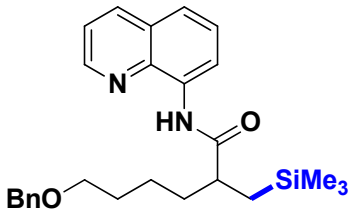
2-((1*S*,4*R*)-bicyclo[2.2.1]heptan-2-yl)-*N*-(quinolin-8-yl)-3-(trimethylsilyl)propanamide 6q

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.85 (br, 1H), 9.81 (br, 1H), 8.83-8.76 (m, 2H), 8.16 (d, *J* = 8.0 Hz, 1H), 7.56-7.44 (m, 3H), 2.27-2.09 (m, 3H), 1.81-1.74 (m, 1H), 1.60-1.27 (m, 5H), 1.11-0.81 (m, 3H), -0.01 (d, *J* = 6.1 Hz, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 175.10, 174.84, 148.36, 138.65, 138.61, 136.43, 136.42, 134.63, 128.10, 127.64, 121.67, 121.38, 121.35, 116.66, 116.63, 51.12, 50.59, 48.96, 48.81, 39.89, 39.29, 37.22, 37.08, 36.86, 36.22, 35.85, 35.76, 30.56, 30.37, 28.81, 20.86, 18.19, -1.12, -1.17; **HRMS** (ESI-TOF) calcd for $C_{22}H_{30}N_2OSi$ $(M)^+$: 366.2127, found: 366.2124.



2-(2-chlorobenzyl)-*N*-(quinolin-8-yl)-3-(trimethylsilyl)propanamide 6t

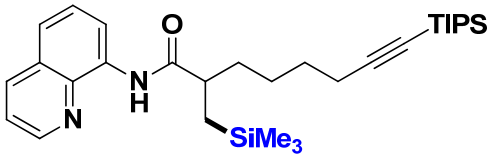
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.66 (br, 1H), 8.74-8.72 (m, 2H), 8.11 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.52-7.44 (m, 2H), 7.40 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.33-7.31 (m, 1H), 7.26-7.23 (m, 1H), 7.04-7.02 (dd, 2H), 3.20 (dd, *J* = 13.2, 8.4 Hz, 1H), 3.04 (dd, *J* = 13.2, 6.2 Hz, 1H), 3.01-2.94 (m, 1H), 1.26 (dd, *J* = 14.8, 9.2 Hz, 1H), 0.90 (dd, *J* = 14.8, 4.8 Hz, 1H), 0.03 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 174.35, 148.23, 138.50, 137.38, 136.28, 134.53, 134.16, 131.76, 129.63, 127.96, 127.93, 127.49, 126.82, 121.62, 121.46, 116.60, 44.93, 40.67, 20.73, -1.02; **HRMS** (EI-TOF) calcd for $C_{22}H_{25}ClN_2OSi$ (M^+): 396.1425, found: 396.1429.



6-(benzyloxy)-*N*-(quinolin-8-yl)-2-((trimethylsilyl)methyl)hexanamide 6r

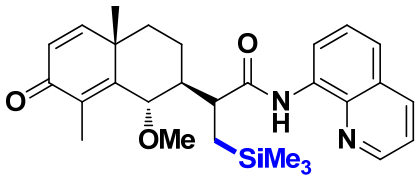
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.86 (br, 1H), 8.81-8.78 (m, 2H), 8.16 (d, *J* = 8.0 Hz, 1H), 7.56-7.44 (m, 3H), 7.28-7.23 (m, 5H), 4.45 (s, 2H), 3.46-3.42 (m, 2H), 2.59-2.52 (m, 1H), 1.90-1.81 (m, 1H), 1.68-1.60 (m, 3H), 1.52-1.46 (m, 2H), 1.13 (dd, *J* = 14.8, 8.8 Hz, 1H), 0.87 (dd, *J* = 14.8, 6.0 Hz,

1H), 0.03 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 175.49, 148.32, 138.74, 138.63, 136.45, 134.71, 128.44, 128.09, 127.76, 127.63, 127.57, 121.69, 121.42, 116.62, 73.01, 70.33, 45.26, 36.55, 29.92, 24.38, 21.13, -0.94; **HRMS** (EI-TOF) calcd for $C_{26}H_{34}N_2O_2Si$ (M^+): 434.2390, found: 434.2397.



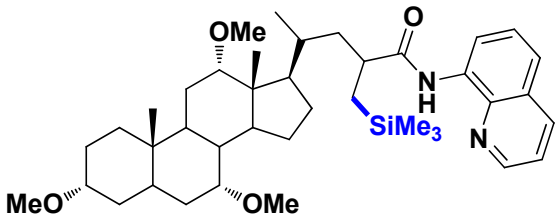
***N*-(quinolin-8-yl)-8-(triisopropylsilyl)-2-((trimethylsilyl)methyl)oct-7-ynamide 6s**

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.85 (br, 1H), 8.83-8.79 (m, 2H), 8.16 (d, *J* = 8.4 Hz, 1H), 7.56-7.44 (m, 3H), 2.58-2.51 (m, 1H), 2.22 (t, *J* = 6.4 Hz, 2H), 1.88-1.79 (m, 1H), 1.60-1.42 (m, 7H), 1.14 (dd, *J* = 14.4, 8.8 Hz, 1H), 1.04-0.94 (m, 21H), 0.88 (dd, *J* = 14.4, 8.8 Hz ,1H), 0.03 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 175.54, 148.30, 138.63, 136.45, 134.71, 128.10, 127.62, 121.68, 121.39, 116.62, 109.26, 80.21, 45.30, 36.63, 28.94, 28.85, 27.22, 21.14, 19.93, 18.77, 11.44, -0.93; **HRMS** (EI-TOF) calcd for $C_{30}H_{48}N_2OSi_2$ (M^+):508.3305, found: 508.3299.



(*R*)-2-((1*S*,2*S*,4*aS*)-1-methoxy-4a,8-dimethyl-7-oxo-1,2,3,4,4a,7-hexahydronaphthalen-2-yl)-*N*-(quinolin-8-yl)-3-(trimethylsilyl)propanamide 6u

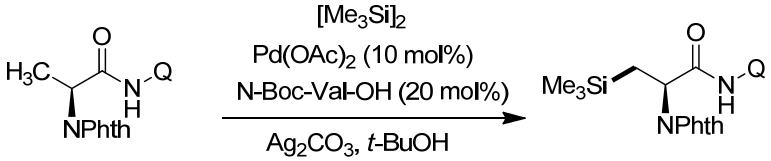
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.91 (br, 1H), 8.83 (dd, *J* = 4.0, 1.6 Hz, 1H), 8.75 (dd, *J* = 7.2, 1.2 Hz, 1H), 8.14 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.54-7.43 (m, 3H), 6.68 (d, *J* = 10.0 Hz, 1H), 6.21 (d, *J* = 10.0 Hz, 1H), 4.03 (d, *J* = 11.2 Hz, 1H), 3.32-3.26 (m, 4H), 2.20 (s, 3H), 2.17-2.11 (m, 1H), 1.84-1.79 (m, 3H), 1.31(s, 3H), 1.22-1.15 (m, 1H), 0.60 (dd, *J* = 14.0, 1.6 Hz, 1H), 0.05 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 187.25, 173.90, 157.33, 156.55, 148.38, 138.60, 136.42, 134.82, 129.50, 128.09, 127.51, 125.95, 121.73, 121.43, 116.50, 82.39, 58.42, 50.10, 44.08, 42.54, 39.23, 22.79, 21.65, 12.23, 10.31, -1.13; **HRMS** (EI-TOF) calcd for $C_{28}H_{36}N_2O_3Si$ (M^+): 476.2495, found: 476.2495.



(4*R*)-*N*-(quinolin-8-yl)-4-((3*R*,7*R*,10*S*,12*S*,13*R*,17*R*)-3,7,12-trimethoxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[a]phenanthren-17-yl)-2-((trimethylsilyl)methyl)pentanamide 6v

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.84 (br, 1H), 8.83 (d, *J* = 4.0 Hz, 1H), 8.78 (d, *J* = 7.2 Hz, 1H), 8.15 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.55-7.44 (m, 3H), 3.38 (s, 1H), 3.32 (s, 3H), 3.23 (s, 3H), 3.20 (s, 3H), 3.14 (d, *J* = 2.0 Hz, 1H), 3.02-2.95 (m, 1H), 2.60-2.55 (m, 1H), 2.18 (dd, *J* = 24.8, 12.8 Hz, 1H), 2.11-1.43 (m, 15H), 1.34-1.15 (m, 4H), 1.07-0.83 (m, 10H), 0.69 (s, 3H), 0.02 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 176.18, 148.30, 138.65, 136.42, 134.87, 128.08, 127.63, 121.65, 121.28, 116.58, 82.16, 80.87, 77.10, 55.99, 55.84, 55.51, 47.54, 46.47, 43.19, 42.90, 42.81, 42.12, 39.79, 35.41, 35.06, 34.56, 34.37, 28.13, 28.00, 27.93, 26.88, 23.36, 23.02, 22.13, 19.78, 17.96, 12.66, -0.98; **HRMS** (EI-TOF) calcd for $C_{40}H_{62}N_2O_4Si$ (M^+): 662.4479, found: 662.4484.

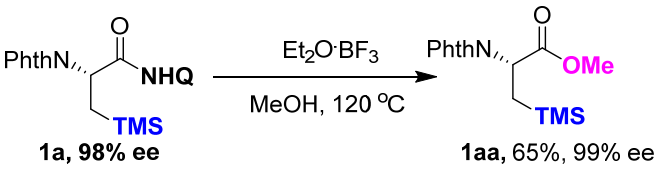
2.4 Gram-scale reaction



1, 3 mmol, 1.036 g **1a, 1.00 g, 80 %**

To an oven-dried 50 mL screw-capped vial was added substrate **1** (3 mmol), **2a** hexamethyldisilane (15 mmol), $Pd(OAc)_2$ (69 mg, 0.3 mmol), N-Boc-Val-OH (129.75 mg, 0.6 mmol), Ag_2CO_3 (1.656 g, 6 mmol), *t*-BuOH (30 mL). The mixture was stirred for 10 h at 125 °C under air followed by cooling. The resulting mixture was filtered through a celite pad and concentrated in *vacuo*. The residue was purified by column chromatography using hexane/EtOAc as the eluent to afford the product (1.0 g, 80%) **1a.**

2.5 Removal of directing group

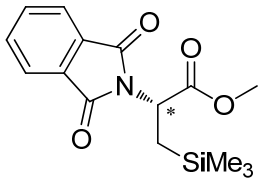


1a, 98% ee **1aa,** 65%, 99% ee

(*R*)-methyl 2-(1,3-dioxoisoindolin-2-yl)-3-(trimethylsilyl)propanoate 1aa

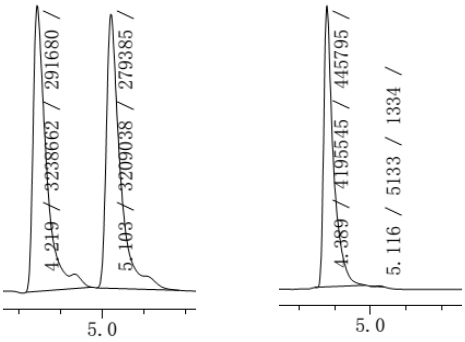
To an oven-dried 50 mL screw-capped vial was added **1** (0.10 mmol), $Et_2O{\cdot}BF_3$ (2.0 mmol) and MeOH (1mL). The mixture was stirred for 20 h at 120 °C under air followed by cooling. The resulting mixture was filtered through a celite pad and concentrated in *vacuo*. The residue was purified by preparing TLC using hexane/EtOAc=5:1 as the eluent to afford the product **1a** (18.5 mg, 62%)**.** **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88-7.83 (m, 2H), 7.75-7.71 (m, 2H), 4.95 (dd, *J*=11.6, 4.8, 1H), 3.71 3.71 (s, 3H), 1.71 (dd, *J*=15.2, 11.6, 1H), 1.54 (dd, *J*=15.2, 4.8, 1H), -0.04 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.24, 167.72, 134.32, 131.98, 123.64, 52.94, 49.32, 17.21, -1.47; HPLC Chiralpack® AD-H column (n-hexane/isopropanol = 70:30, 1.0 mL/min) t_r = 4.389 min (major), t_r = 5.116 min (minor): 99% ee.

***DL*-/*L*-1aa**



Chiral stationary phase: Chiralpack® AD-H, n-hexane/isopropanol = 70:30, 1.0 mL/min

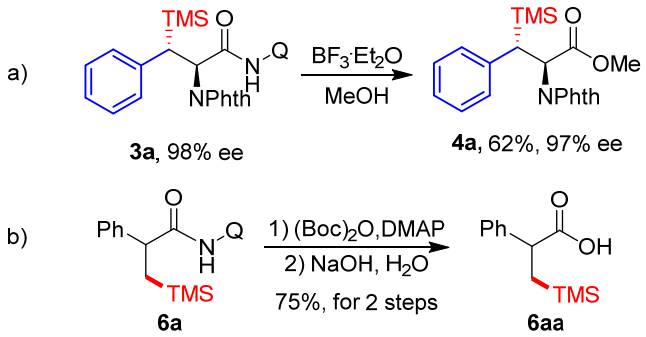
Signal: VWD1 A, Wavelength = 220 nm



Area% report for *DL*/*L*-1aa:

***DL*-1aa**			***L*-1aa**		
Retention Time (min)	Area (mAU*s)	Area %	Retention Time (min)	Area (mAU*s)	Area %

4.219	3238662	50.23	4.389	4195545	99.88
5.103	3209038	49.77	5.116	5133	0.12
Totals	6447700	100.00	Totals	4200677	100.00

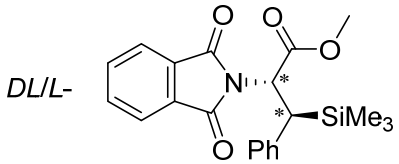


Scheme S1. Removal of AQ auxiliary

(2*R*,3*S*)-methyl 2-(1,3-dioxoisoindolin-2-yl)-3-phenyl-3-(trimethylsilyl)propanoate 4a

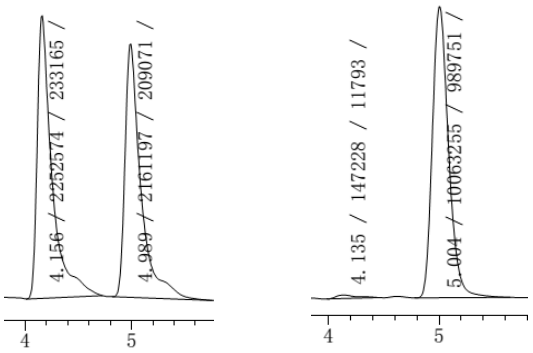
To an oven-dried 50 mL screw-capped vial was added **2a** (0.10 mmol), $Et_2O{\cdot}BF_3$ (2.0 mmol) and MeOH (1mL). The mixture was stirred for 20 h at 120 °C under air followed by cooling. The resulting mixture was filtered through a celite pad and concentrated in *vacuo*. The residue was purified by preparing TLC using hexane/EtOAc=5:1 as the eluent to afford the product **4a** (25.1 mg, 66%)**.** **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68-7.65 (m, 2H), 7.61-7.58 (m, 2H), 7.06 (t, *J* = 7.6 Hz, 2H), 6.97-6.90 (m, 3H), 5.42 (d, *J* = 13.6 Hz, 1H), 3.75 (s, 3H), 3.58 (d, *J* = 13.6 Hz, 1H), 0.02 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.98, 167.60, 140.13, 133.98, 131.49, 128.26, 125.42, 123.34, 54.24, 52.85, 36.26, -1.21. HPLC Chiralpack® AD-H column (n-hexane/isopropanol = 70:30, 1.0 mL/min) t_r = 4.135 min (minor), t_r = 5.004 min (major): 97% ee.

***DL*-/*L*-4a**



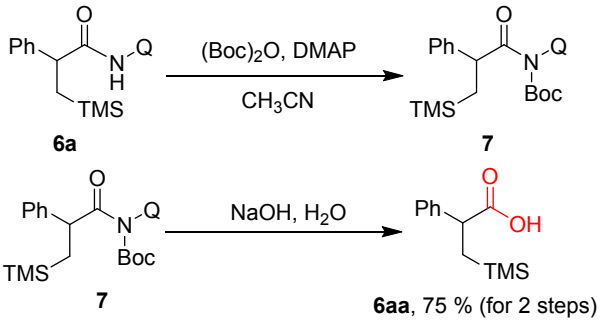
Chiral stationary phase: Chiralpack® AD-H, n-hexane/isopropanol = 70:30, 1.0 mL/min

Signal: VWD1 A, Wavelength = 220 nm



Area% report for *DL*/*L*-3aa:

***DL*-3aa**			***L*-3aa**		
Retention Time (min)	Area (mAU*s)	Area %	Retention Time (min)	Area (mAU*s)	Area %
4.156	2252574	51.04	4.135	147228	1.44
4.989	2161197	48.96	5.004	10063255	98.56
Totals	4413771	100.00	Totals	10210484	100.00



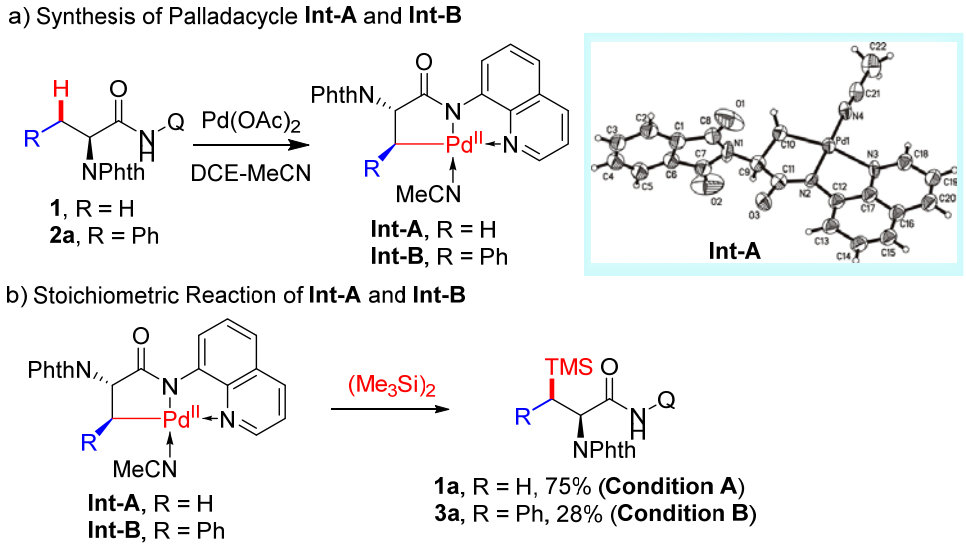
6a (0.470 mmol) was placed in a 50 mL round-bottomed flask, and the flask was flushed with nitrogen. Dichloromethane (5.0 mL) and Boc_2O (0.825 g, 3.78 mmol) were added. *N*,*N*-Dimethyl-4-aminopyridine (0.287 g, 2.35 mmol) was added in one portion and the resulting solution was refluxed for 30 h. The reaction mixture was concentrated in vacuo, followed by column chromatography on silica gel (hexane/ethyl acetate) gave **7**. [4] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.88 (d, *J* = 2.4 Hz, 1H), 8.16 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.80 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.49 (t, *J* = 8.0 Hz, 1H), 7.43-7.23 (m, 7H), 1.55 (dd, *J* = 14.8, 6.0 Hz, 1H), 1.31 (dd, *J* = 14.8, 9.6 Hz, 1H), 1.22 (s, 9H), -0.10 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.22, 152.84, 150.28, 144.44, 141.83, 137.50, 135.93, 128.78, 128.59, 128.38, 127.86, 126.94, 126.09, 121.50, 82.24, 47.14, 27.62, 22.10, -1.15.

To an oven-dried 50 mL screw-capped vial was added **7** (0.10 mmol), NaOH (1.0 mmol) and H_2O

(1mL). The mixture was stirred for 20 h at 120 °C under air followed by cooling. The resulting mixture was HCl (1M) and ethyl acetate. The mixture was extracted with EA (10 ml ×2) and dried with Na_2SO_4, then concentrated in *vacuo*. The residue was purified by preparing TLC using hexane/EtOAc as the eluent to afford the product **6aa** (16.6 mg, 75% for 2 steps)**.** [5] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33-7.23 (m, 5H), 3.63 (t, *J* = 8.0 Hz, 1H), 1.36 (dd, *J* = 14.8, 7.2 Hz, 1H), 1.15 (dd, *J* = 14.8, 8.8 Hz, 1H), -0.13 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 181.32, 140.50, 128.69, 128.18, 127.50, 47.56, 21.21, -1.32.

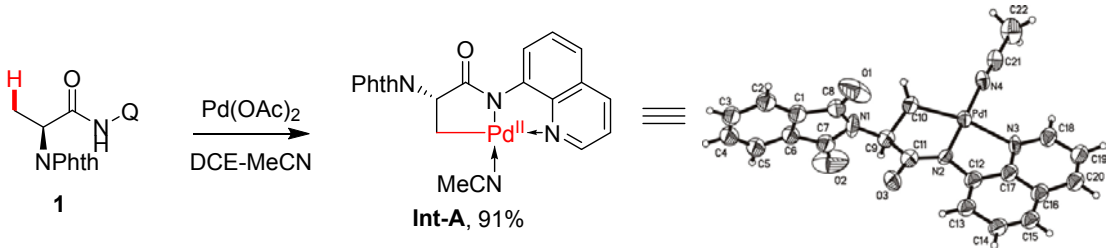
2.6 Mechanistic Investigations

2.6.1 Mechanistic Investigations of Pd-Catalyzed Silylation of α-AAs



Scheme S2. Mechanistic investigations of Pd-catalyzed silylation of α-amino acids

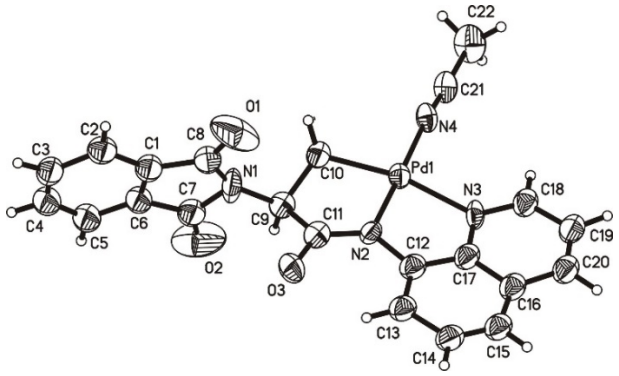
Synthesis of Palladacycle Int-A



$Pd(OAc)_2$ (224.5 mg, 1.0 mmol) and **1** (345.4 mg, 1.0 mmol) were added to CH_3CN/DCE (12 mL+6 mL). The reaction was stirred at 50 ºC for 4 h, and then the solvent was removed under vacuum. To

the crude product, 3 mL of CH_2Cl_2 was added, followed by 10 mL of petroleum ether, and then the purified product was collected by filtration, washed with petroleum ether, and dried under vacuum to afford **Int-A** (446.6 mg, 91%) as a yellow powder. A single crystal suitable for X-ray diffraction was obtained.

X-ray Crystallographic Data of Int-A



Bond precision:	C-C = 0.0192 A	Wavelength=0.71073	
Cell:	a=9.6660(4)	b=15.5081(6)	c=29.565(1)
	alpha=90	beta=90	gamma=90
Temperature:	293 K		

	Calculated	Reported
Volume	4431.8(3)	4431.8(3)
Space group	P b c a	P b c a
Hall group	-P 2ac 2ab	-P 2ac 2ab
Moiety formula	C22 H16 N4 O3 Pd	C22 H16 N4 O3 Pd
Sum formula	C22 H16 N4 O3 Pd	C22 H16 N4 O3 Pd
Mr	490.79	490.79
Dx,g cm-3	1.471	1.471
Z	8	8
Mu (mm-1)	0.866	0.866
F000	1968.0	1968.0
F000'	1960.73	
h,k,lmax	11,18,35	11,18,35
Nref	4065	4055
Tmin,Tmax	0.724,0.785	0.712,0.794
Tmin'	0.688	

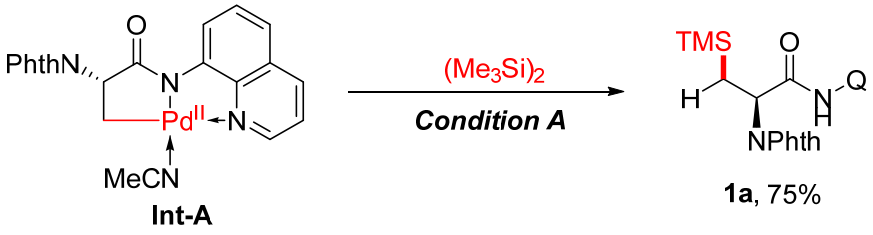
Correction method= MULTI-SCAN

Data completeness= 0.998 Theta(max)= 25.350

R(reflections)= 0.1026(2962) wR2(reflections)= 0.2389(4055)

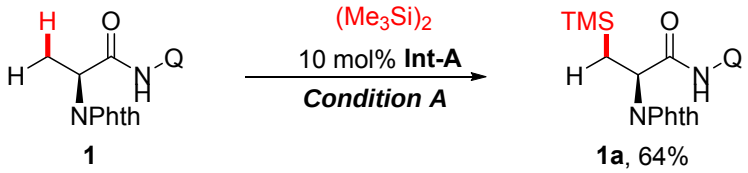
S = 1.057 Npar= 276

Stoichimetric reaction of intermediate Int-A



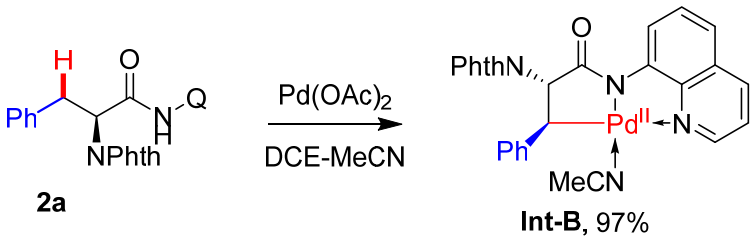
To an oven-dried 50 mL screw-capped vial was added substrate **Int-A** (0.05 mmol), hexamethyldisilane (0.25 mmol), Ag_2CO_3 (0.025 mmol), 2,6-diMeO-BQ (0.075 mmol), 1,4-dioxane (1.0 mL). The mixture was stirred for 12 h at 125 °C under air followed by cooling. The resulting mixture was filtered through a celite pad and concentrated in *vacuo*. The residue was purified by preparative TLC using hexane/EtOAc as the eluent to afford the product **1a** was obtained in 75% yield (determined by ^{1}H NMR).

Catalytic reaction of intermediate Int-A



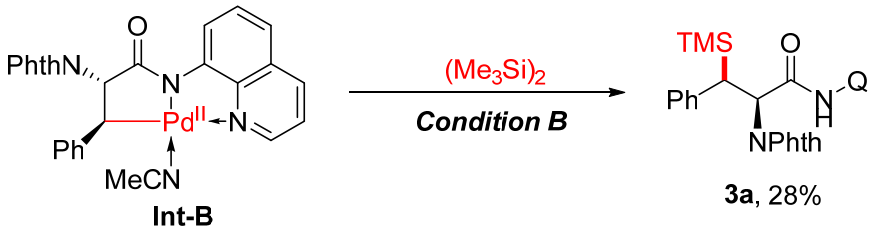
To an oven-dried 50 mL screw-capped vial was added substrate **1** (0.1 mmol), hexamethyldisilane (0.5 mmol), **Int-A** (0.01 mmol), Ag_2CO_3 (0.05 mmol), 2,6-diMeO-BQ (0.15 mmol), 1,4-dioxane (1.0 mL). The mixture was stirred for 12 h at 125 °C under air followed by cooling. The resulting mixture was filtered through a celite pad and concentrated in *vacuo*. The residue was purified by preparative TLC using hexane/EtOAc as the eluent to afford the product **1a** was obtained in 64% yield (determined by ^{1}H NMR).

Synthesis of the Palladacycle Int-B[6]



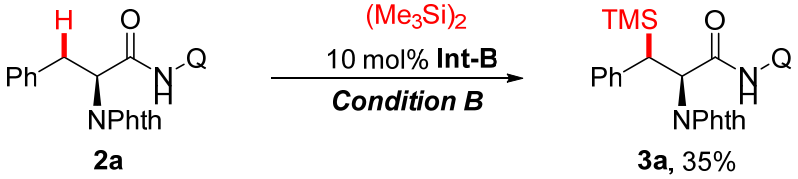
$Pd(OAc)_2$ (224.5 mg, 1.0 mmol) and **2a** (421.5 mg, 1.0 mmol) were added to CH_3CN/DCE (12 mL+6 mL). The reaction was stirred at 50 °C for 4 h, and then the solvent was removed under vacuum. To the crude product, 3 mL of CH_2Cl_2 was added, followed by 10 mL of petroleum ether, and then the purified product was collected by filtration, washed with petroleum ether, and dried under vacuum to afford **Int-B** (550.2 mg, 97% yield, dr > 25:1 estimated by ^{1}H NMR) as a yellow powder. INT-D is a known compound.[6]

Stoichimetric reaction of intermediate Int-B



To an oven-dried 50 mL screw-capped vial was added substrate **Int-B** (0.05 mmol), hexamethyldisilane (0.25 mmol), Ag_2CO_3 (0.025 mmol), 2,6-diMeO-BQ (0.075 mmol), 1,4-dioxane (1.0 mL). The mixture was stirred for 12 h at 125 °C under air followed by cooling. The resulting mixture was filtered through a celite pad and concentrated in *vacuo*. The residue was purified by preparative TLC using hexane/EtOAc as the eluent to afford the product **3a** was obtained in 28% yield (determined by ^{1}H NMR).

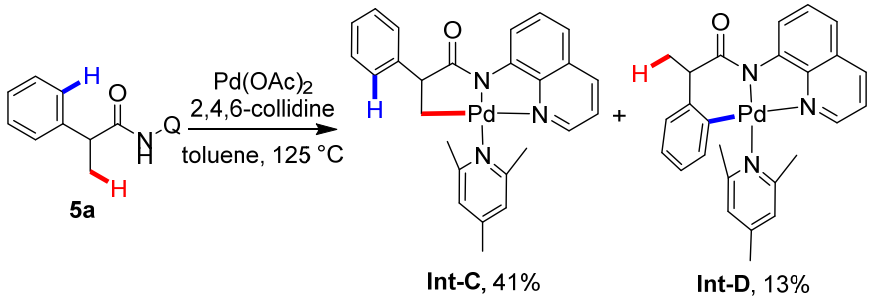
Catalytic reaction of intermediate Int-B



To an oven-dried 50 mL screw-capped vial was added substrate **2a** (0.1 mmol), hexamethyldisilane (0.5 mmol), **Int-B** (0.015 mmol), Ag_2CO_3 (0.05 mmol), 2,6-diMeO-BQ (0.15 mmol), 1,4-dioxane (1.0 mL). The mixture was stirred for 12 h at 125 °C under air followed by cooling. The resulting mixture was filtered through a celite pad and concentrated in *vacuo*. The residue was purified by preparative TLC using hexane/EtOAc as the eluent to afford the product **3a** was obtained in 35% yield (determined by ^{1}H NMR).

2.6.2 Experimental Investigations of the Origin of Site-Selective C-H Silylation of 2-APA

Synthesis of Int-C and Int-D

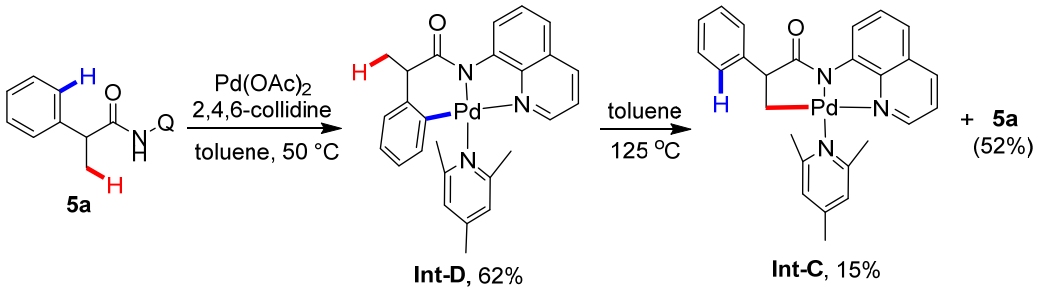


To an oven-dried 50 mL screw-capped vial was added substrate **1a** (0.1 mmol), ligand (0.2 mmol), $Pd(OAc)_2$ (0.1 mmol) in toluene (1 mL). The mixture was stirred for 12 h at 125 °C under N_2 followed by cooling. The resulting mixture was concentrated in *vacuo*. The residue was purified by preparative TLC using DCM/MeOH as the eluent to afford **Int-C** (20.6 mg, 41%) and **Int-D** (6.5 mg, 13%). **Int-C** and **Int-D** were yellow-brownish solids that are stable at ambient temperature and decomposed slowly in solution.

Int-C: ^{1}**H NMR** (400 MHz, $CDCl_3$) δ 9.16 (d, *J* = 8.0 Hz, 1H), 8.14 (d, *J* = 8.4 Hz, 1H), 7.61 (d, *J* = 3.6 Hz, 1H), 7.50-7.45 (m, 3H), 7.28-7.23 (m, 3H), 7.21-7.14 (m, 2H), 7.00 (s, 1H), 6.96 (s, 1H), 4.01 (t, *J* = 7.6 Hz, 1H), 3.12 (s, 3H), 3.00 (s, 3H), 2.32 (s, 3H), 1.88 (t, *J* = 8.8 Hz, 1H), 1.57 (dd, *J* = 9.2, 7.2 Hz, 1H); ^{13}**C NMR** (100 MHz, $CDCl_3$) δ 185.62, 159.39, 159.37, 149.41, 147.53, 146.86, 145.79, 145.05, 137.82, 130.03, 129.30, 128.21, 128.06, 125.53, 123.38, 120.98, 120.62, 118.21, 60.10, 27.58, 27.48, 20.84, 14.22; **HRMS** (ESI-TOF) calcd for $C_{26}H_{26}N_3OPd$ $(M+H)^+$: 502.1105, found: 502.1101.

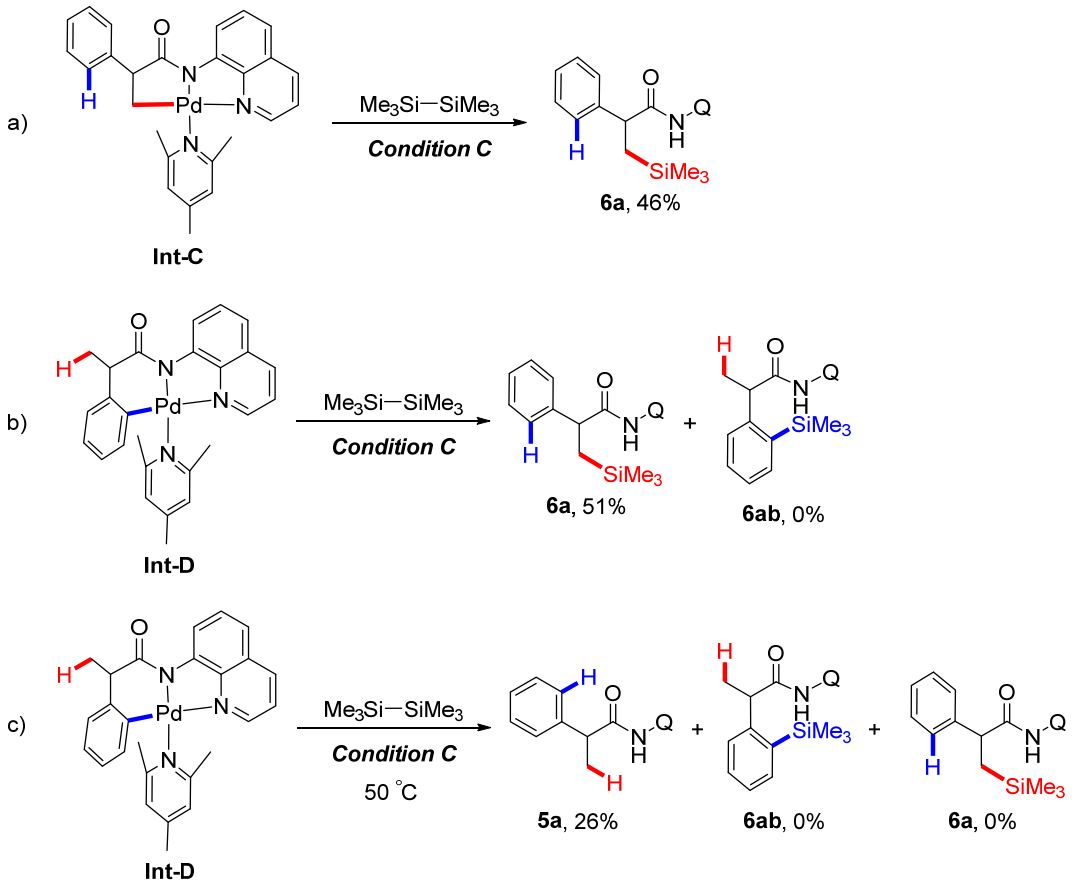
Int-D: ^{1}**H NMR** (400 MHz, $CDCl_3$) δ 8.95 (d, *J*=8.0, 1H), 8.20 (dd, *J*=8.0, 1.2, 1H), 7.57 (t, *J*=8.0, 1H), 7.32-7.29 (m, 2H), 7.21-7.18 (m, 2H), 7.10 (s, 1H), 7.05 (d, *J*=7.2, 1H), 6.93 (t, *J*=6.8, 1H), 6.66 (td, *J*=7.2, 1.2, 1H), 6.22 (dd, *J*=7.2, 0.8, 1H), 4.04 (q, *J*=6.8, 1H), 3.09 (s, 3H), 2.97 (s, 3H), 2.45 (s, 3H), 2.02 (d, *J*=6.8, 3H); ^{13}**C NMR** (100 MHz, $CDCl_3$) δ178.63, 159.95, 158.98, 150.57, 150.47, 148.05, 144.54, 144.31, 141.93, 138.30, 134.31, 129.50, 129.45, 126.02, 125.00, 124.67, 124.50, 124.15,

124.02, 120.61, 118.57, 58.10, 28.52, 27.59, 26.28, 21.09; **HRMS** (ESI-TOF) calcd for $C_{26}H_{26}N_3OPd$ $(M+H)^+$: 502.1105, found: 502.1108.



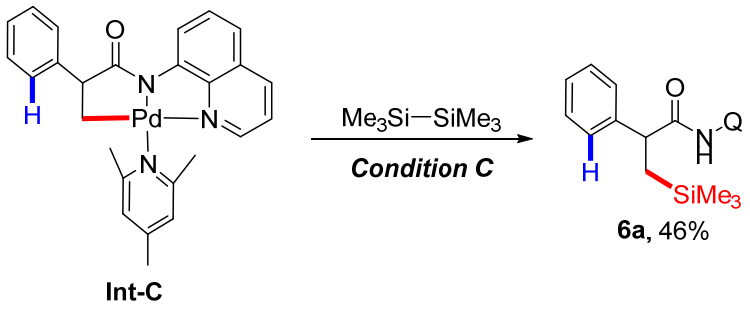
To an oven-dried 50 mL round-bottomed flask was added substrate **5a** (0.5 mmol), 2,4,6-trimethylpyridine (1.0 mmol), $Pd(OAc)_2$ (0.5 mmol) in toluene (10 mL). The flask was flushed with nitrogen and stirred for 12 h at 50 °C under N_2 followed by cooling. The purified product was collected by filtration, washed with toluene, diethyl ether and dried under vacuum to afford a yellow powder, which was a mixture of Int-B and 2,4,6-collidine·HOAc salt. The mixture was purified by preparing TLC (EA:DCM:PE = 4:1:2 as the eluent) to afford **Int-D** (155.6 mg, 62%) as yellow powder.

To an oven-dried 50 mL screw-capped vial was added **Int-D** (0.1 mmol) in toluene (1 mL). The mixture was stirred for 12 h at 125 °C under N_2 followed by cooling. The resulting mixture was concentrated in *vacuo*. The residue was purified by preparative TLC (EA:DCM:PE = 4:1:2 as the eluent) to afford **Int-C** (7.5 mg, 15%) as yellow powder and recovered **5a** (52%).



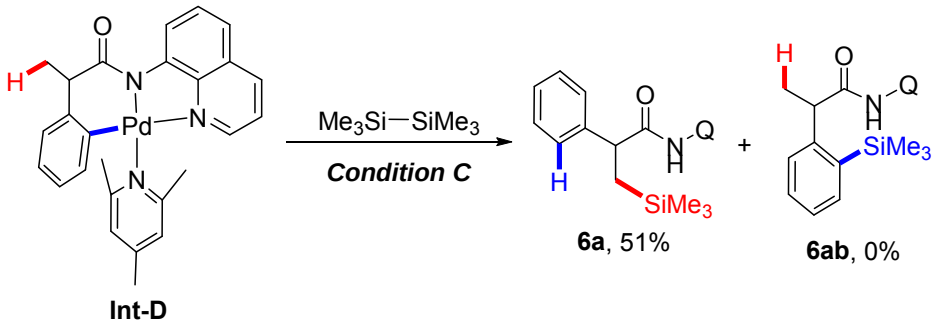
Scheme S3. Stoichimetric reaction of intermediate **Int-C** and **Int-D**

Stoichimetric reaction of intermediate Int-C



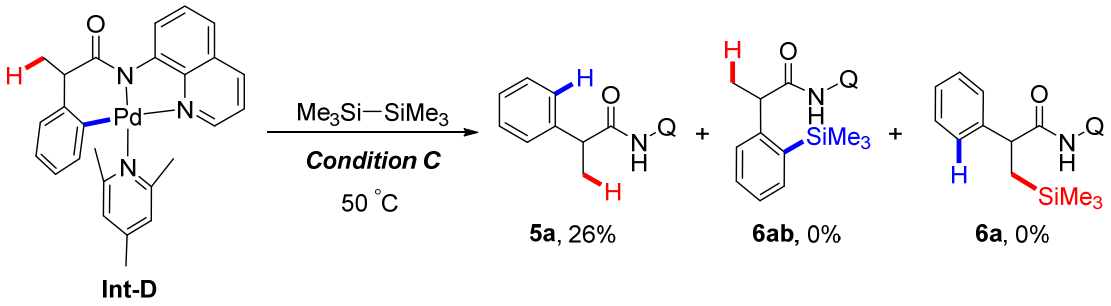
To an oven-dried 50 mL screw-capped vial was added **Int-C** (0.1 mmol), **2** (0.5 mmol), *s*-BINA-PO_2H (0.03 mmol), Ag_2CO_3 (0.2 mmol), $NaHCO_3$ (0.2 mmol), LiOAc (0.05 mmol), toluene (1.0 mL). The mixture was stirred for 10 h at 125 °C under air followed by cooling. The resulting mixture was filtered through a celite pad and concentrated in *vacuo*. The product **6a** was obtained in 46% yield (determined by ^{1}H NMR).

Stoichimetric reaction of intermediate Int-D at 125 °C



To an oven-dried 50 mL screw-capped vial was added **Int-D** (0.1 mmol), **2** (0.5 mmol), *s*-BINA-PO_2H (0.03 mmol), Ag_2CO_3 (0.2 mmol), $NaHCO_3$ (0.2 mmol), LiOAc (0.05 mmol), toluene (1.0 mL). The mixture was stirred for 10 h at 125 °C under air followed by cooling. The resulting mixture was filtered through a celite pad and concentrated in *vacuo*. The product **6a** was obtained in 51% yield and **6ab** (0%) (determined by ^{1}H NMR).

Stoichimetric reaction of intermediate Int-D at 50 °C



To an oven-dried 50 mL screw-capped vial was added **Int-D** (0.05 mmol), **2** (0.25 mmol), *s*-BINA-PO_2H (0.015 mmol), Ag_2CO_3 (0.1 mmol), $NaHCO_3$ (0.1 mmol), LiOAc (0.025 mmol), toluene (1.0 mL). The mixture was stirred for 10 h at 50 °C under air followed by cooling. The resulting mixture was filtered through a celite pad and concentrated in *vacuo*. **5a** was isolated in 26% yield and no silylation products **6a** and **6ab** was observed in crude ^{1}H NMR.

3. References

1. K. Chen, S.-Q. Zhang, J.-W. Xu, B.-F. Shi, *Chem. Commun.* **2014**, *50*, 13924.

2. K. Chen, F. Hu, S.-Q. Zhang, B.-F. Shi, *Chem. Sci.* **2013**, *4*, 3906.

3. W.-H. Rao, B.-B. Zhan, K. Chen, P.-X. Ling, Z.-Z. Zhang, B.-F. Shi, *Org. Lett.* **2015**, *17*, 3552.

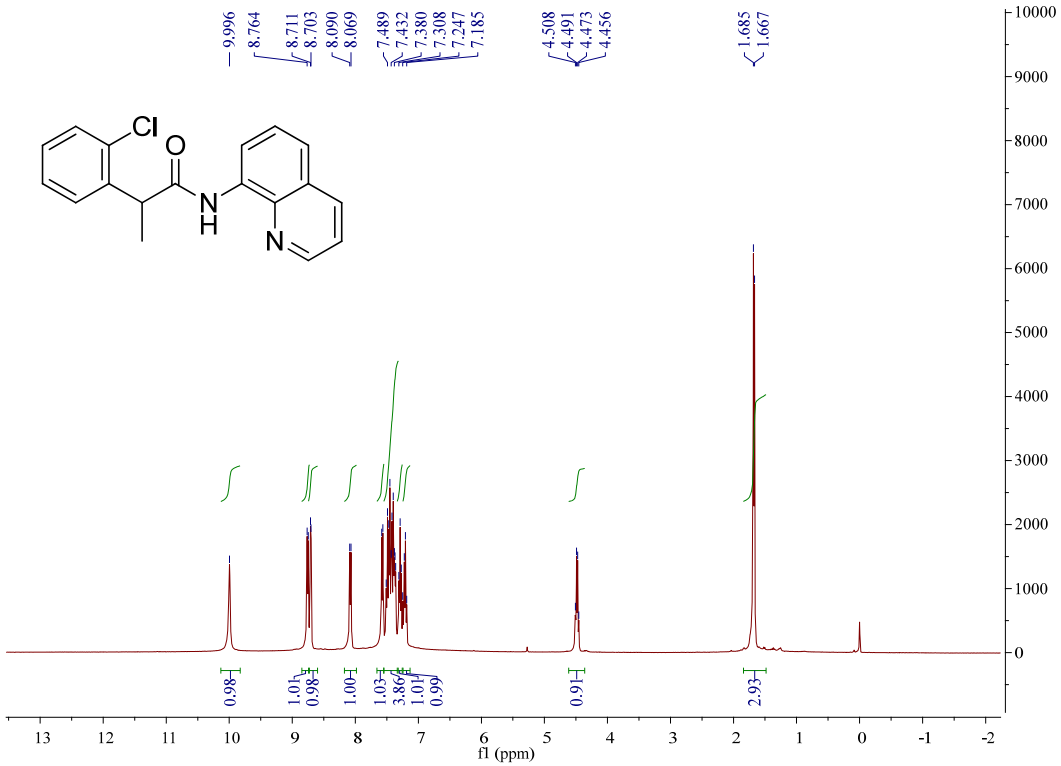
4. K. Chen, S.-Q. Zhang, H.Z. Jiang, J.-W. Xu, B.-F. Shi, *Chem. Eur. J.* **2015**, *21*, 3264**.**

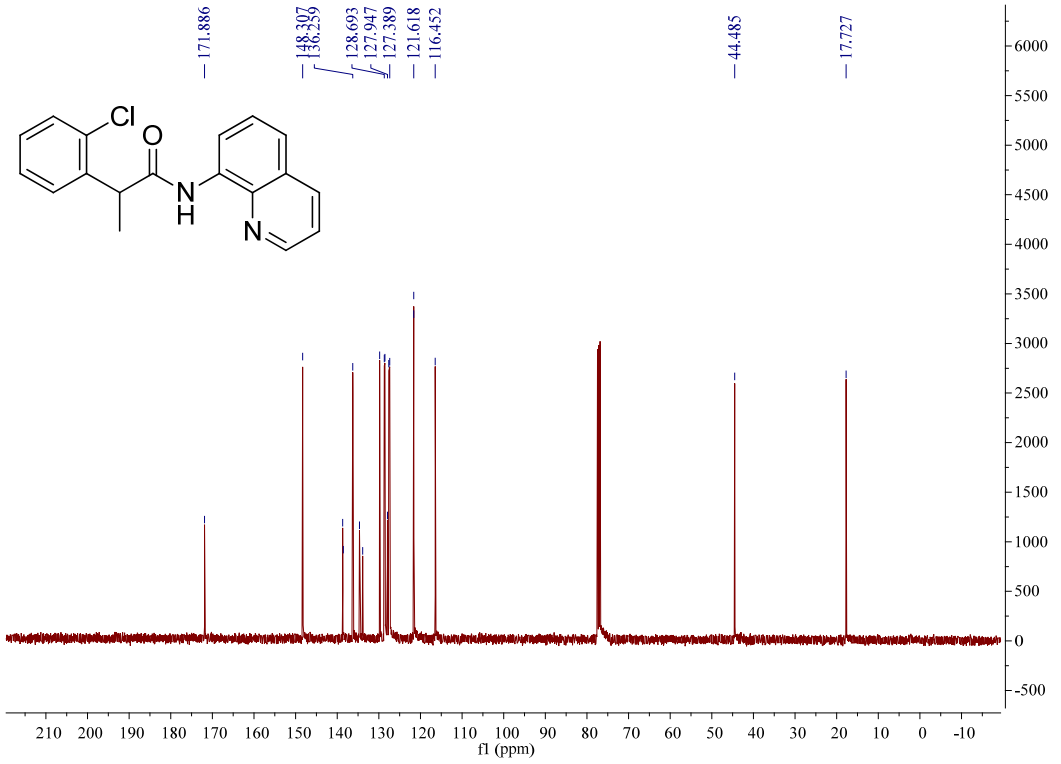
5. S.-Y. Zhang, Q. Li, He, G., Nack, W. A. and Chen, G. *J. Am. Chem. Soc.* **2013**, *135*, 12135.

6. K. Chen, B.-F. Shi, *Angew. Chem. Int. Ed.* **2014**, *53*, 11950.

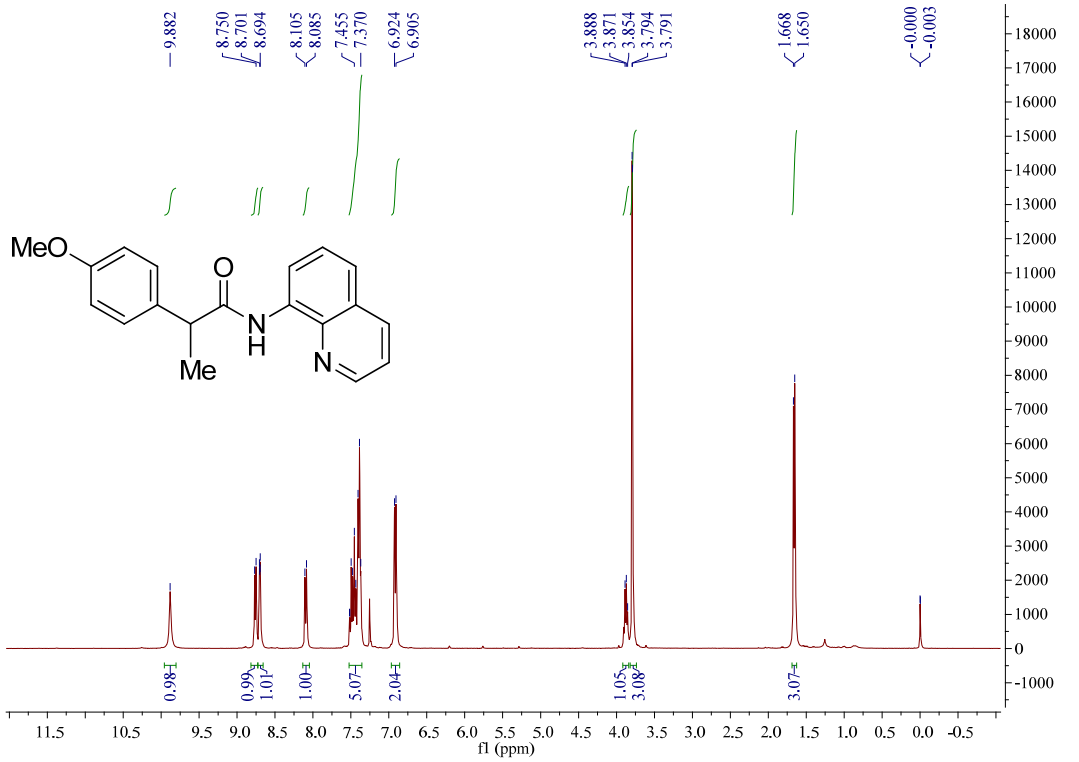
4. NMR Spectra

5d





5h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8.694
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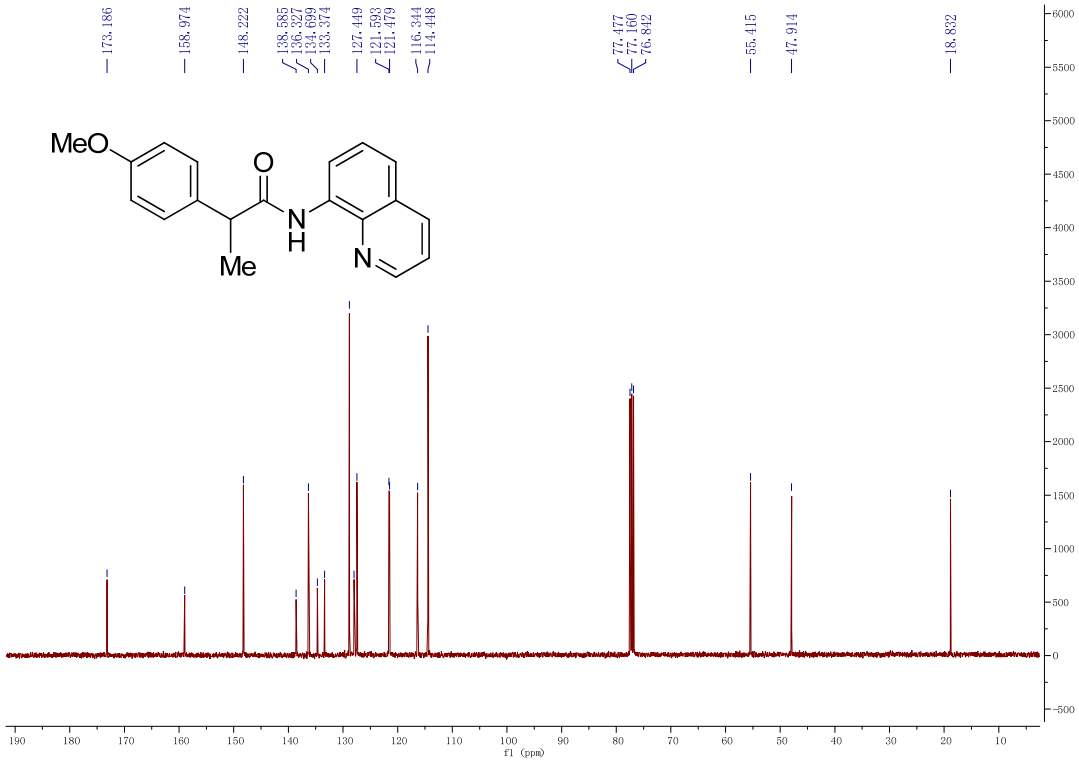
8.085
7.455
7.370
6.924
6.905
3.888
3.871
3.854
3.794
3.791
1.668
1.650
-0.000
-0.003
MeO
O
N
H
Me
N
0.98
0.99
1.01
1.00
5.07
2.04
1.05
3.08
3.07
f1 (ppm)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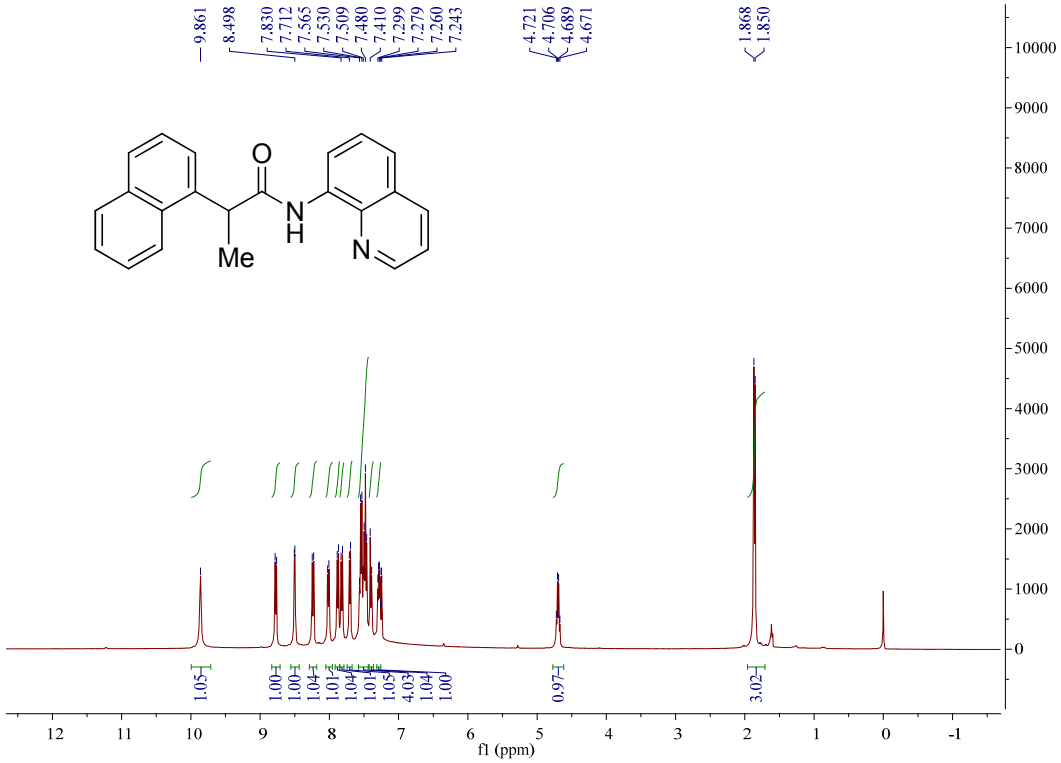
148.222
138.585
136.327
134.699
133.374
127.449
121.593
121.479
116.344
114.448
77.477
77.160
76.842
55.415
47.914
18.832
MeO
O
N
H
Me
N
f1 (ppm)

5j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7.712
7.565
7.530
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7.480
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7.299
7.279
7.260
7.243
4.721
4.706
4.689
4.671
1.868
1.850
O
N
H
Me
N
1.05
1.00
1.00
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1.05
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1.00
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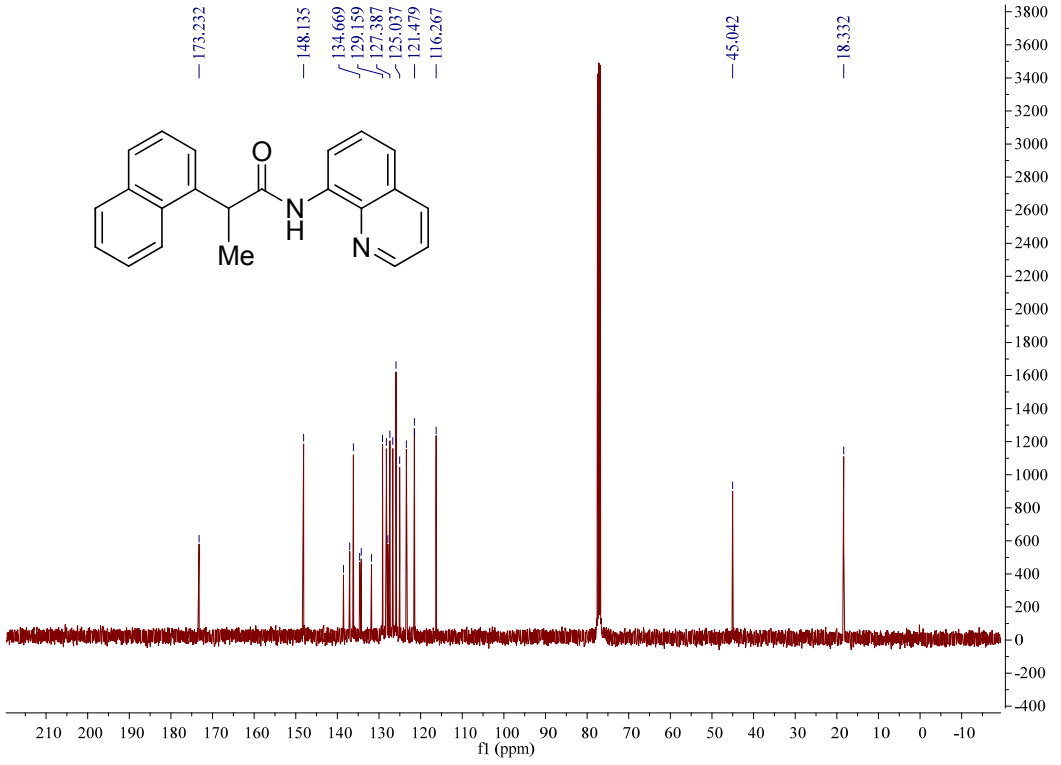
3.02
f1 (ppm)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134.669
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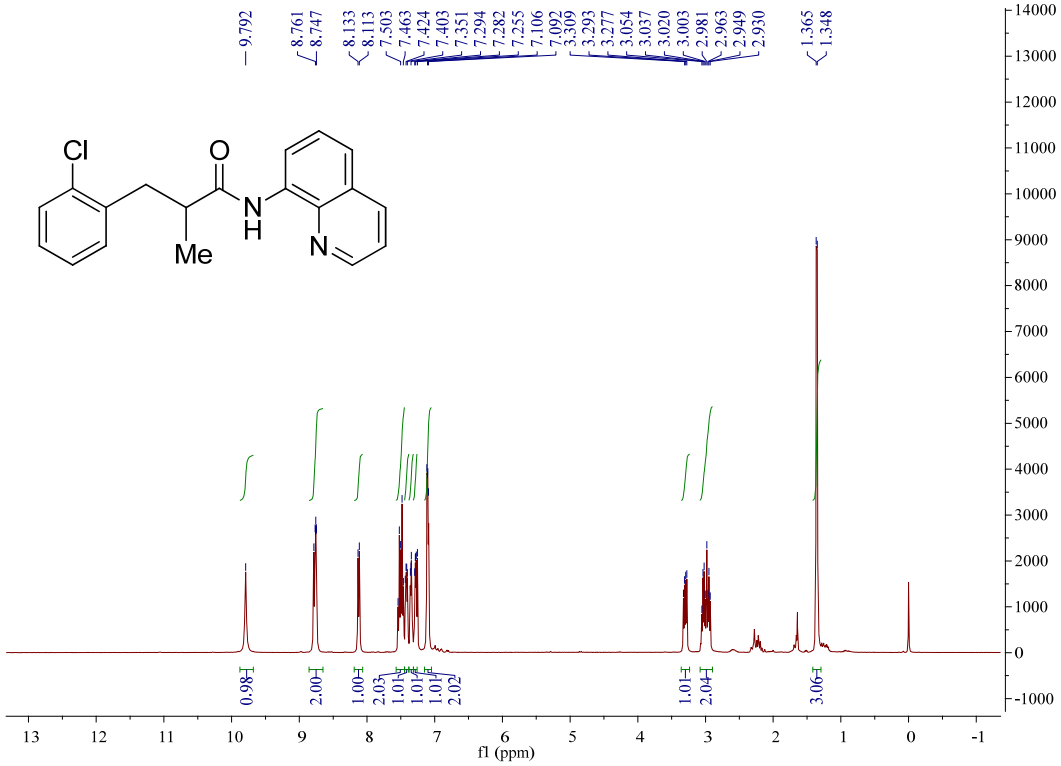
N
H
Me
N
f1 (ppm)

5t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7.255
7.106
7.092
3.309
3.293
3.277
3.054
3.037
3.020
3.003
2.981
2.963
2.949
2.930
1.365
1.348
Cl
O
N
H
Me
N
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2.03
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1.01
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1.01
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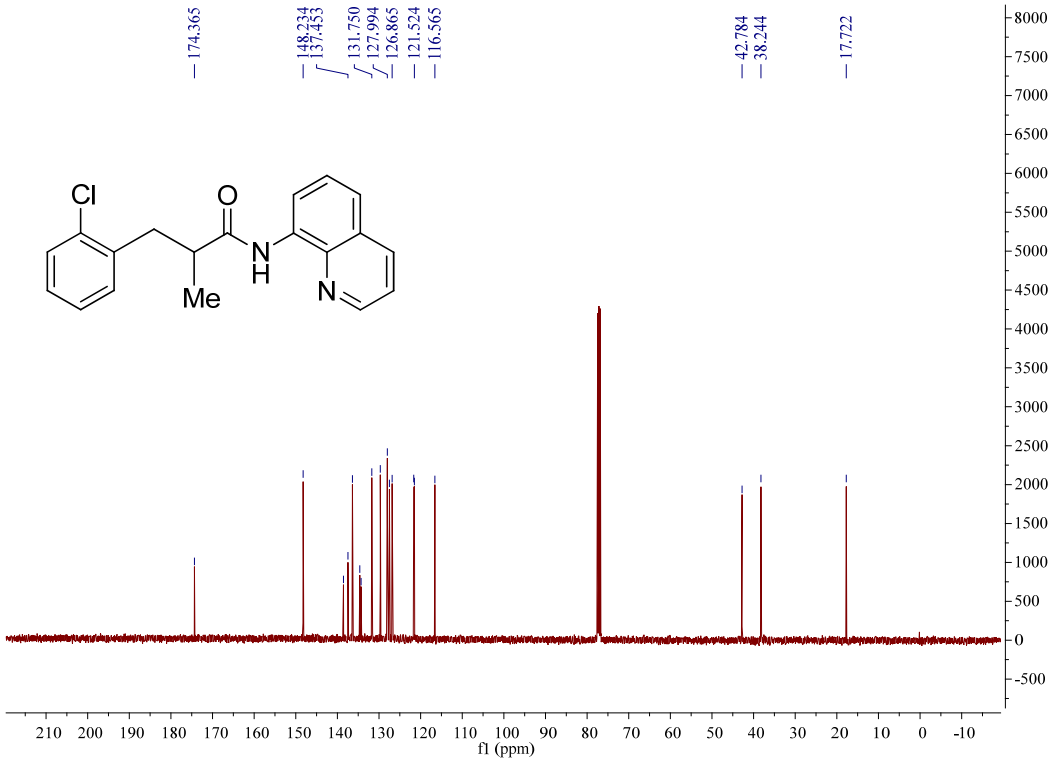
3.06
f1 (ppm)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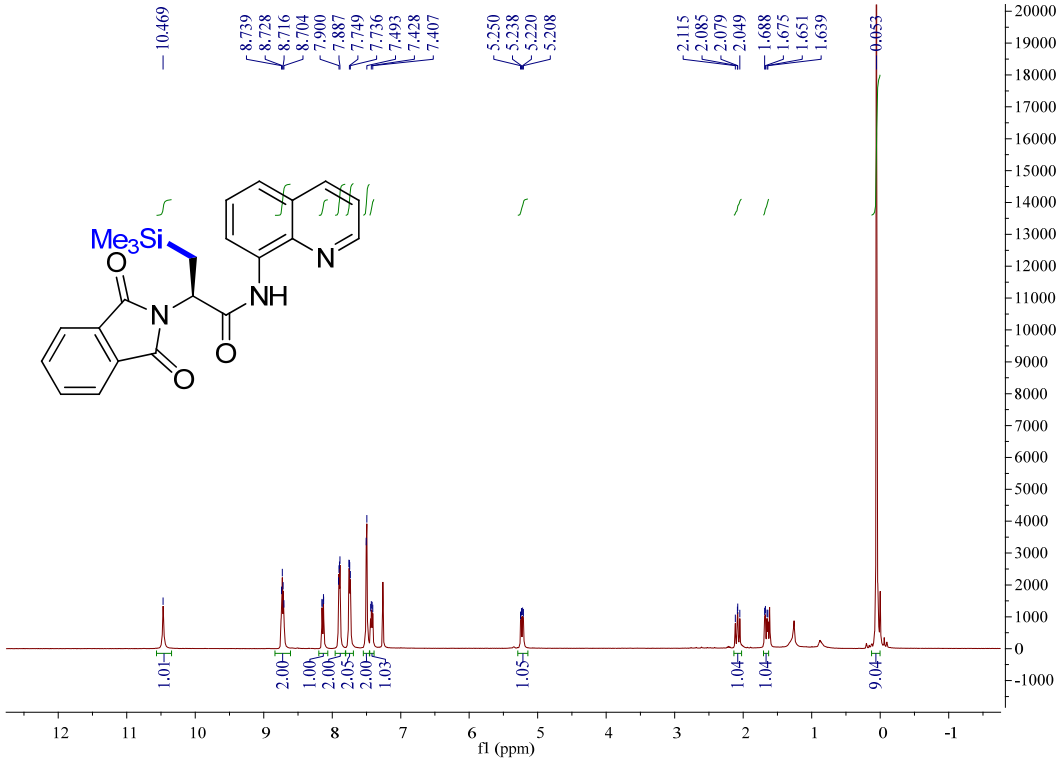
N
H
Me
N
f1 (ppm)

1a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7.407
5.250
5.238
5.220
5.208
2.115
2.085
2.079
2.049
1.688
1.675
1.651
1.639
0.053
Me3Si
O
N
NH
O
N
O
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2.00
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2.00
1.03
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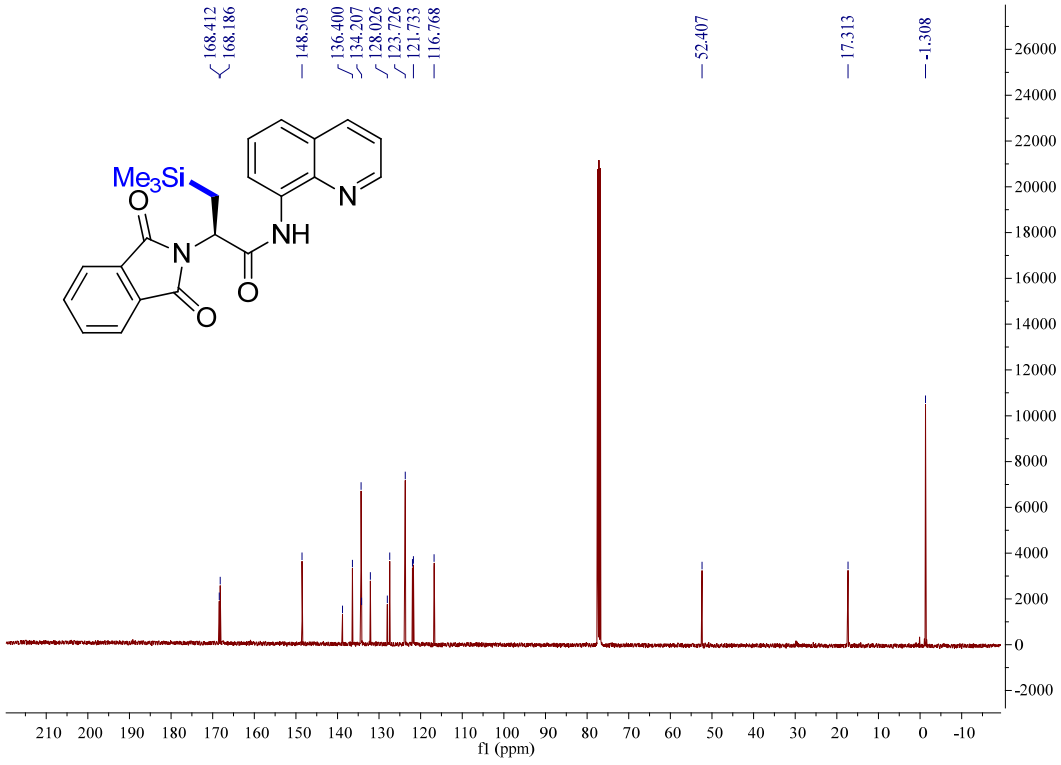
1.04
1.04
9.04
f1 (ppm)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134.207
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123.726
121.733
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52.407
17.313
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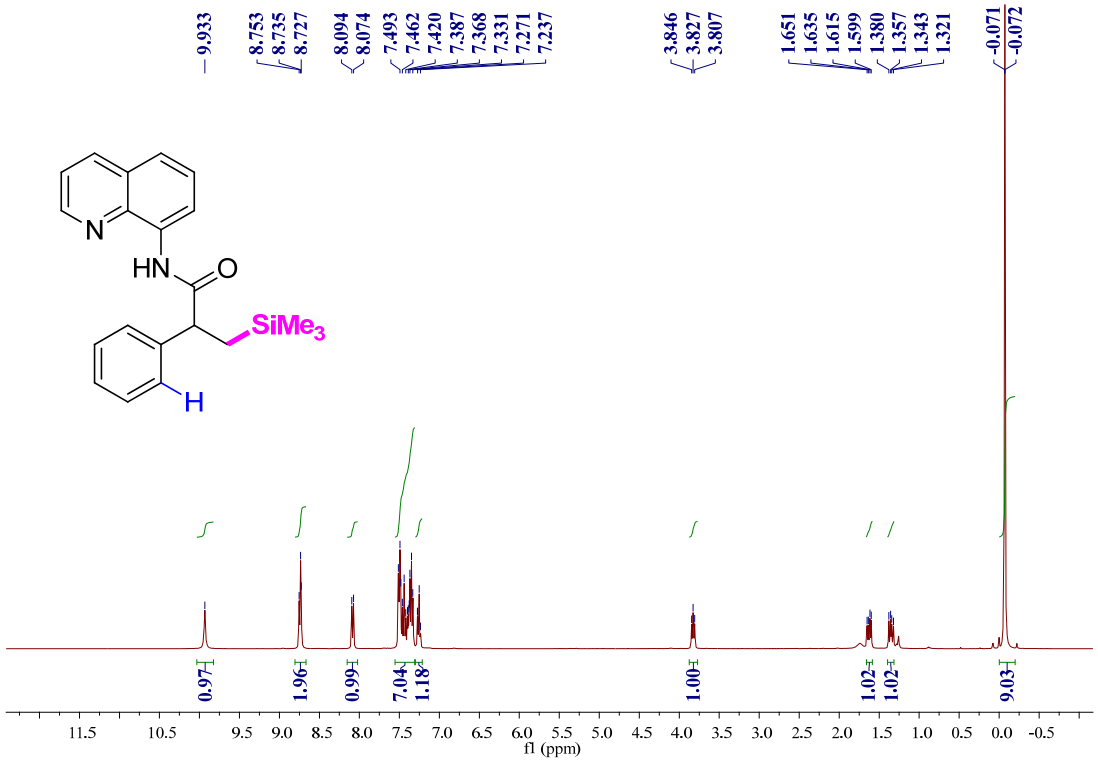
Me3Si
O
N
NH
O
N
O
f1 (ppm)

6a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7.271
7.237
3.846
3.827
3.807
1.651
1.635
1.615
1.599
1.380
1.357
1.343
1.321
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-0.072
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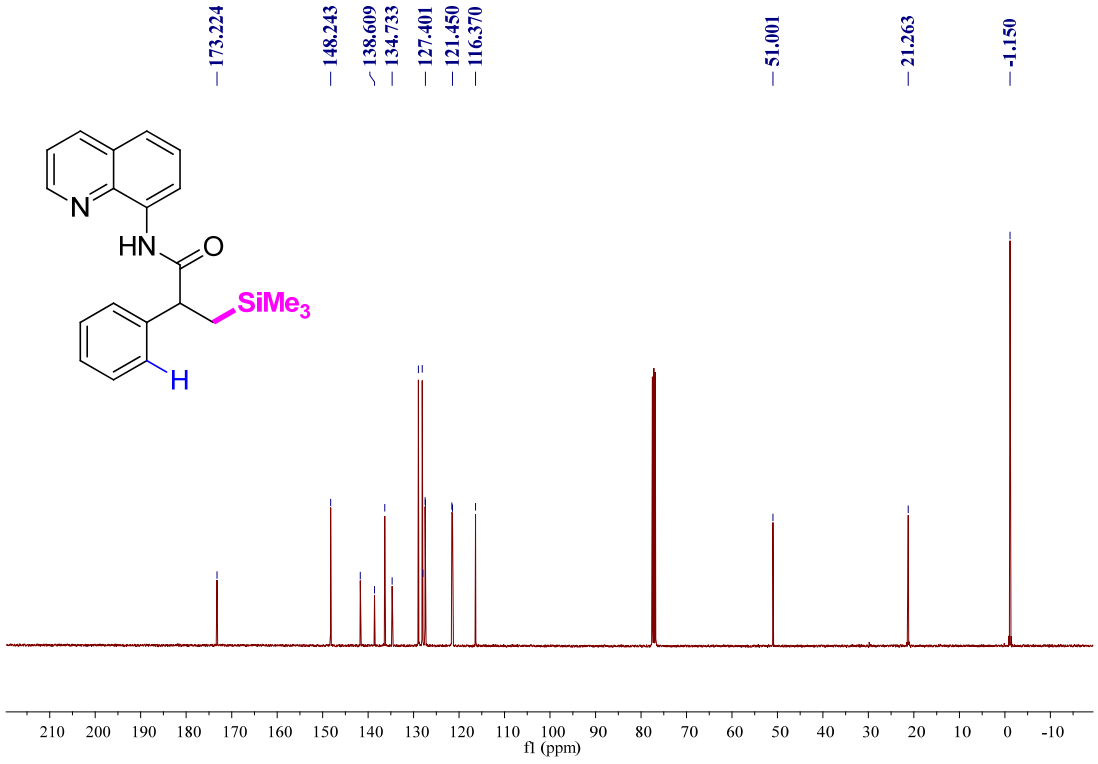
9.03
f1 (ppm)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H
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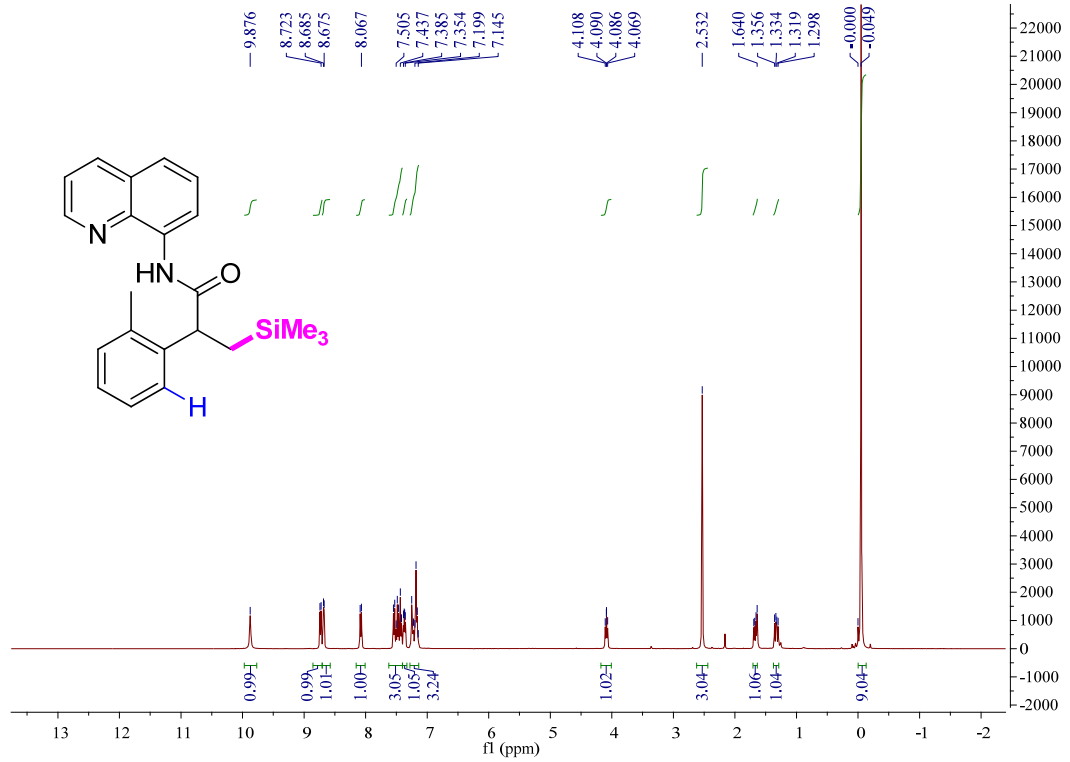
6b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7.199
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4.090
4.086
4.069
2.532
1.640
1.356
1.334
1.319
1.298
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-0.049
0.99
0.99
1.01
1.00
3.05
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O
SiMe3
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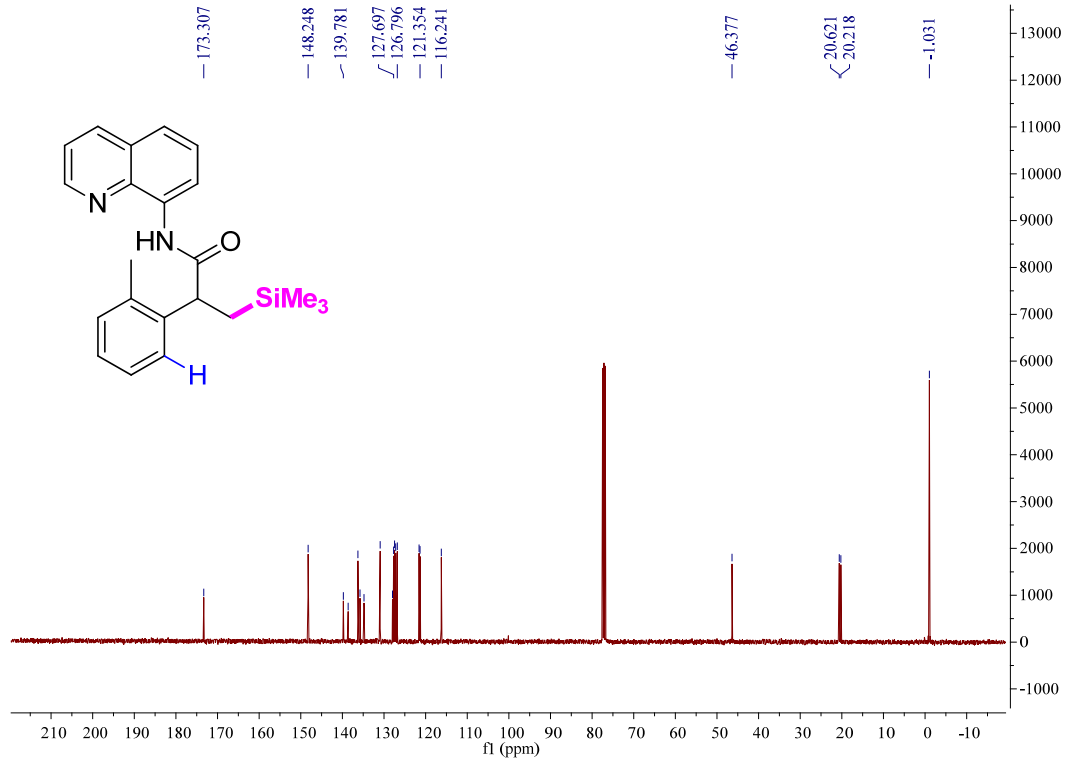
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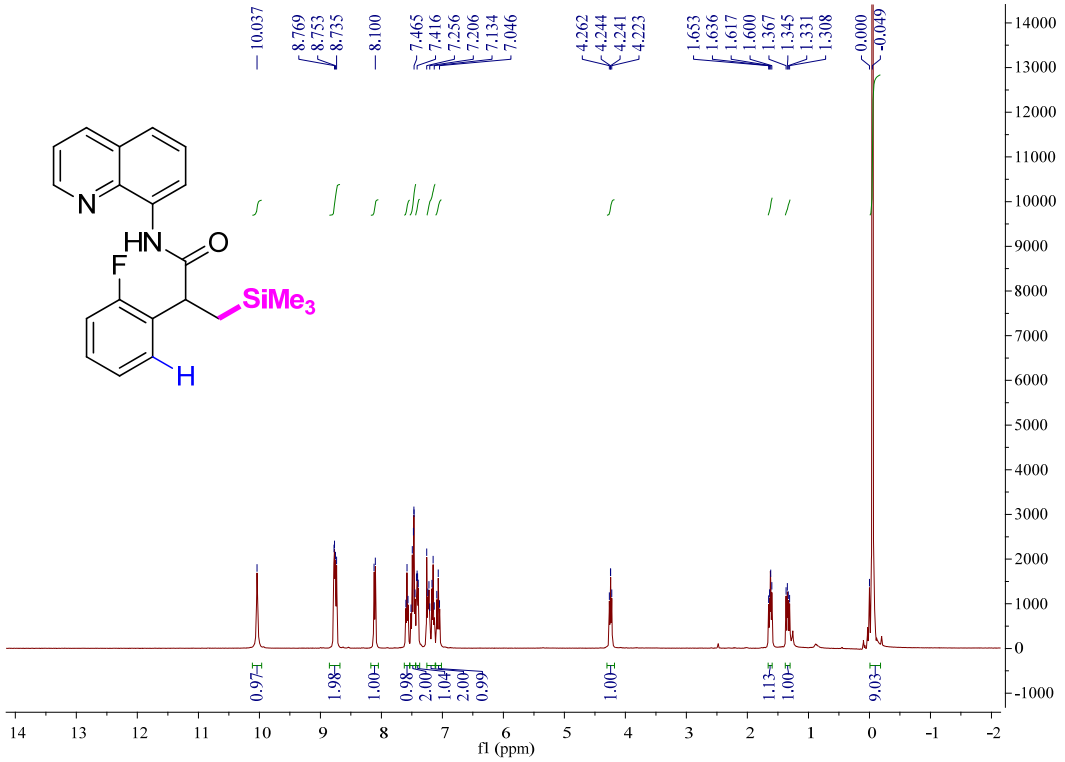
O
SiMe3
H

6c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4.244
4.241
4.223
1.653
1.636
1.617
1.600
1.367
1.345
1.331
1.308
0.000
-0.049
0.97
1.98
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2.00
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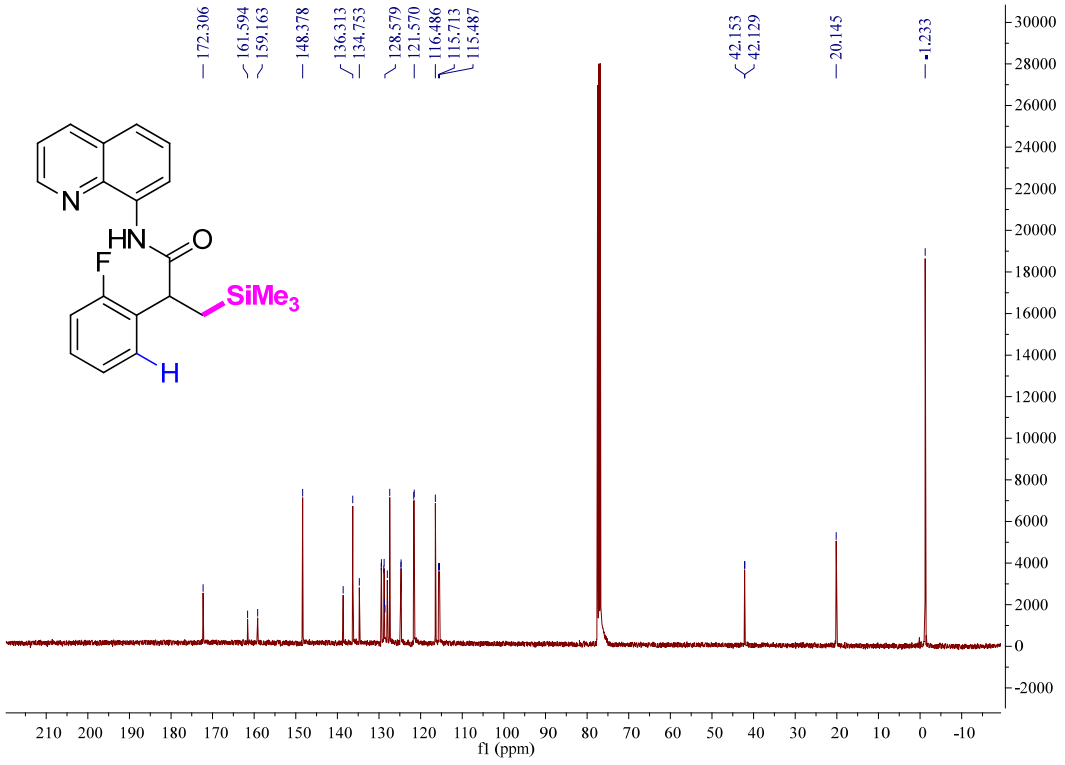
1.00
9.03
F1 (ppm)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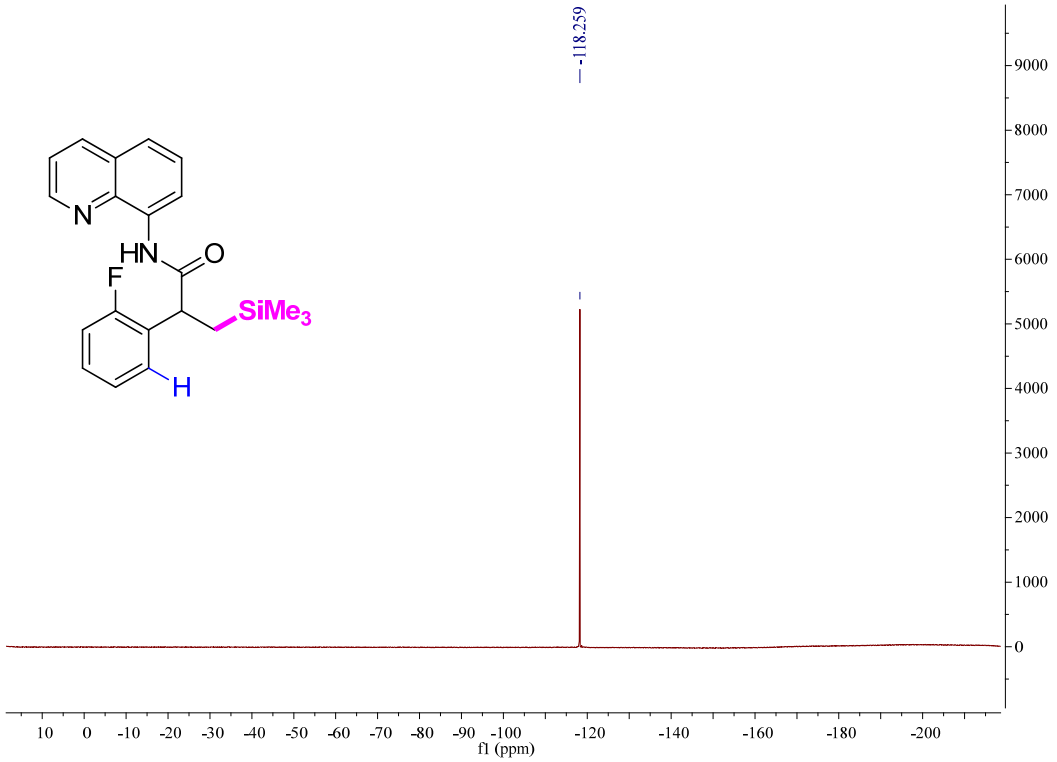
F1 (ppm)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7000
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5000
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3000
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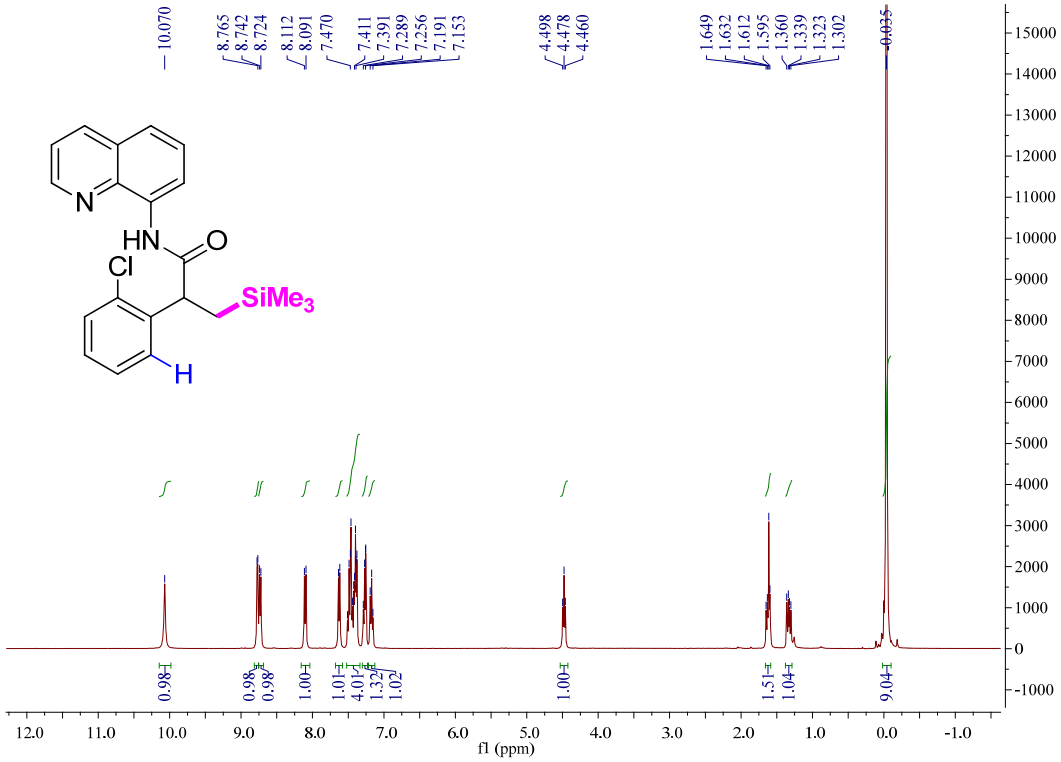
1000
0
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

6d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7.256
7.191
7.153
4.498
4.478
4.460
1.649
1.632
1.612
1.595
1.360
1.339
1.323
1.302
0.035
N
HN
O
Cl
SiMe3
H
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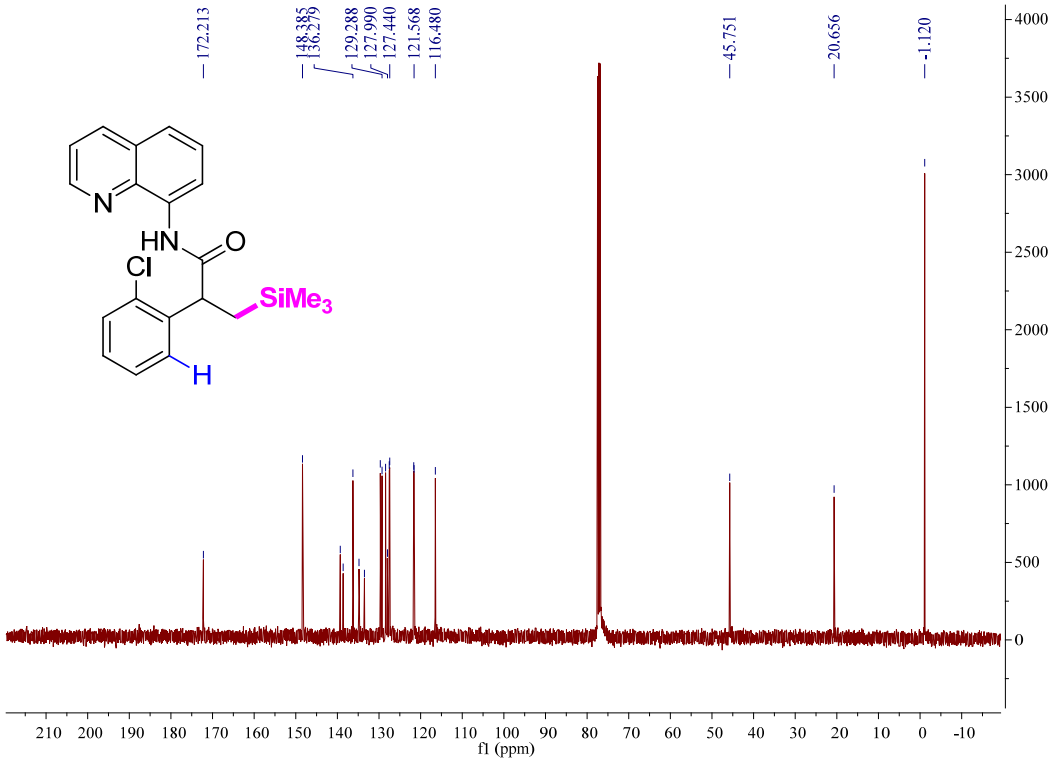
f1 (ppm)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Cl
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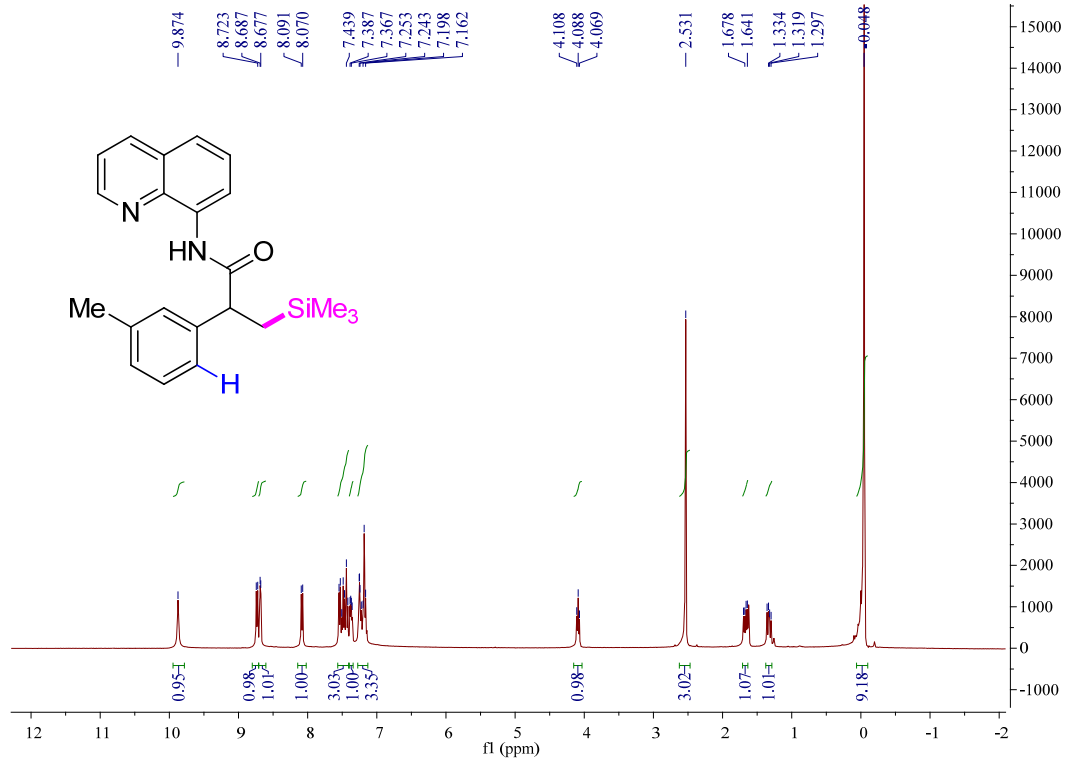
H
f1 (ppm)

6e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7.253
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7.198
7.162
4.108
4.088
4.069
2.531
1.678
1.641
1.334
1.319
1.297
0.048
0.95
0.98
1.01
1.00
3.03
1.00
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3.02
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1.01
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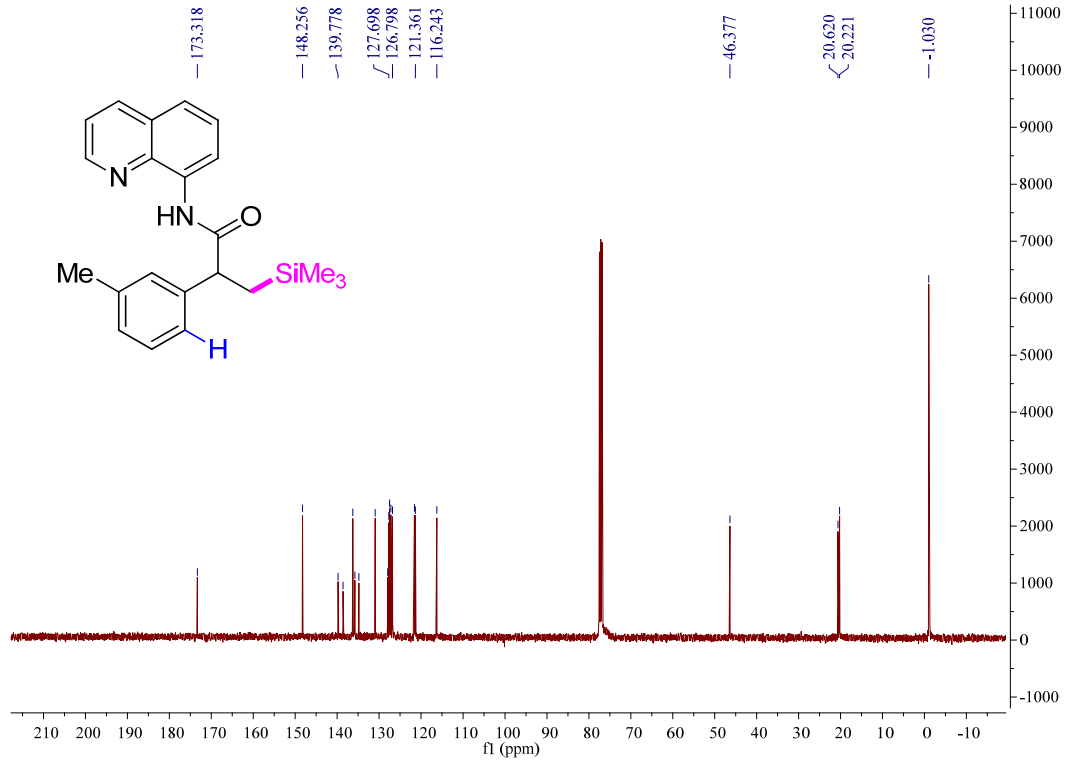
HN
O
Me
SiMe3
H
f1 (ppm)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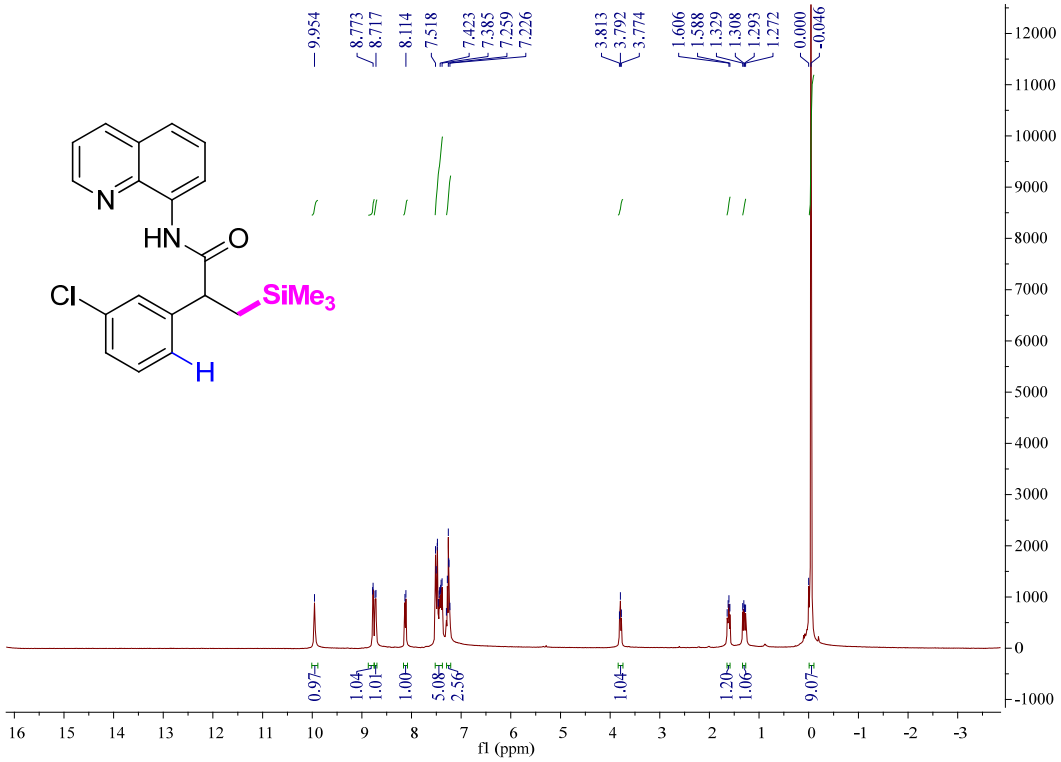
HN
O
Me
SiMe3
H
f1 (ppm)

6f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7.226
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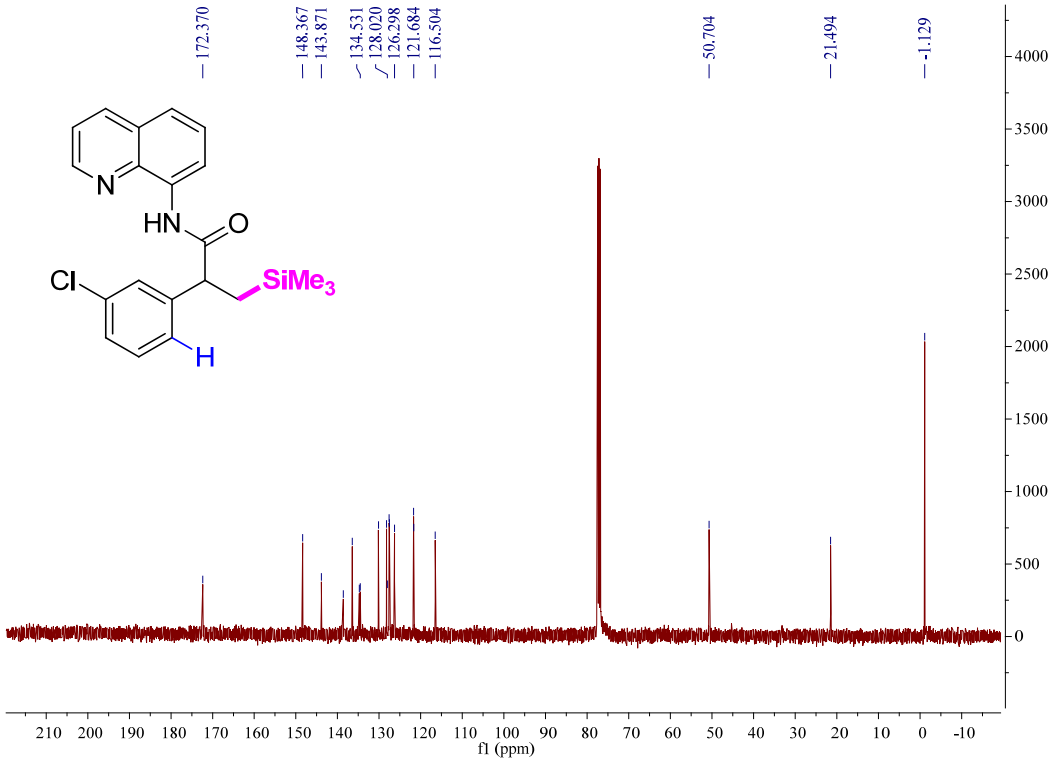
3.792
3.774
1.606
1.588
1.329
1.308
1.293
1.272
0.000
-0.046
0.97
1.04
1.01
1.00
5.08
2.56
1.04
1.20
1.06
9.07
f1 (ppm)
N
HN
O
Cl
SiMe3
H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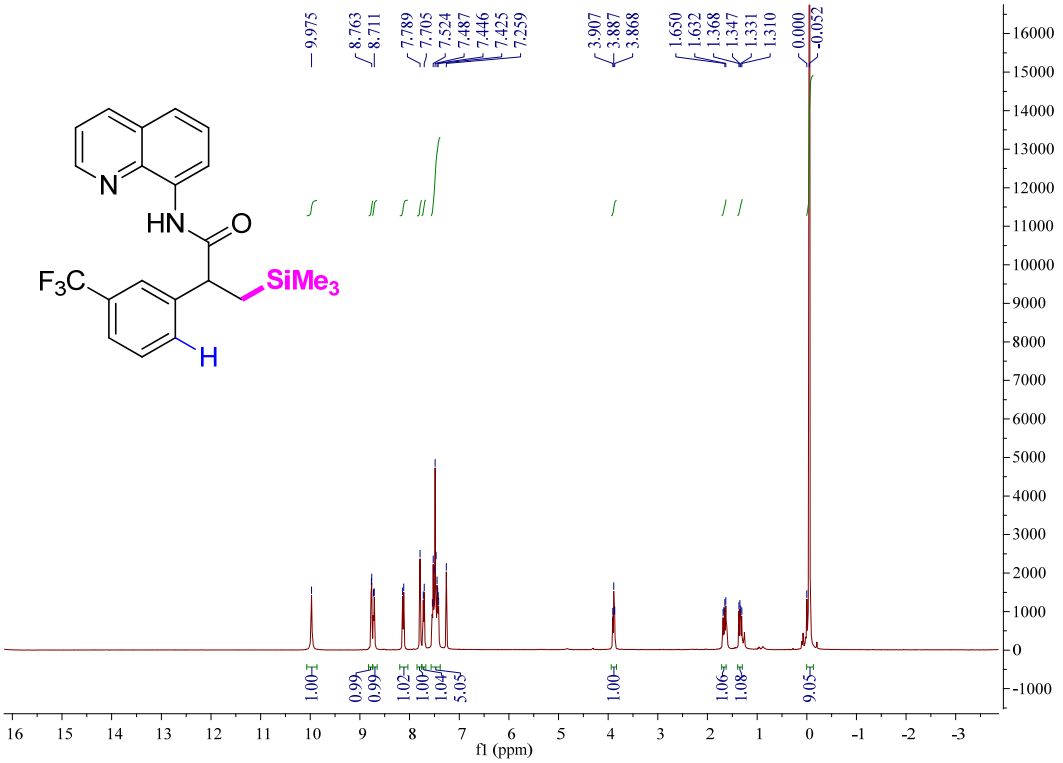
O
Cl
SiMe3
H

6g


9.975
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7.487
7.446
7.425
7.259
3.907
3.887
3.868
1.650
1.632
1.368
1.347
1.331
1.310
0.000
-0.052
1.00
0.99
0.99
1.02
1.00
1.04
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1.00
1.06
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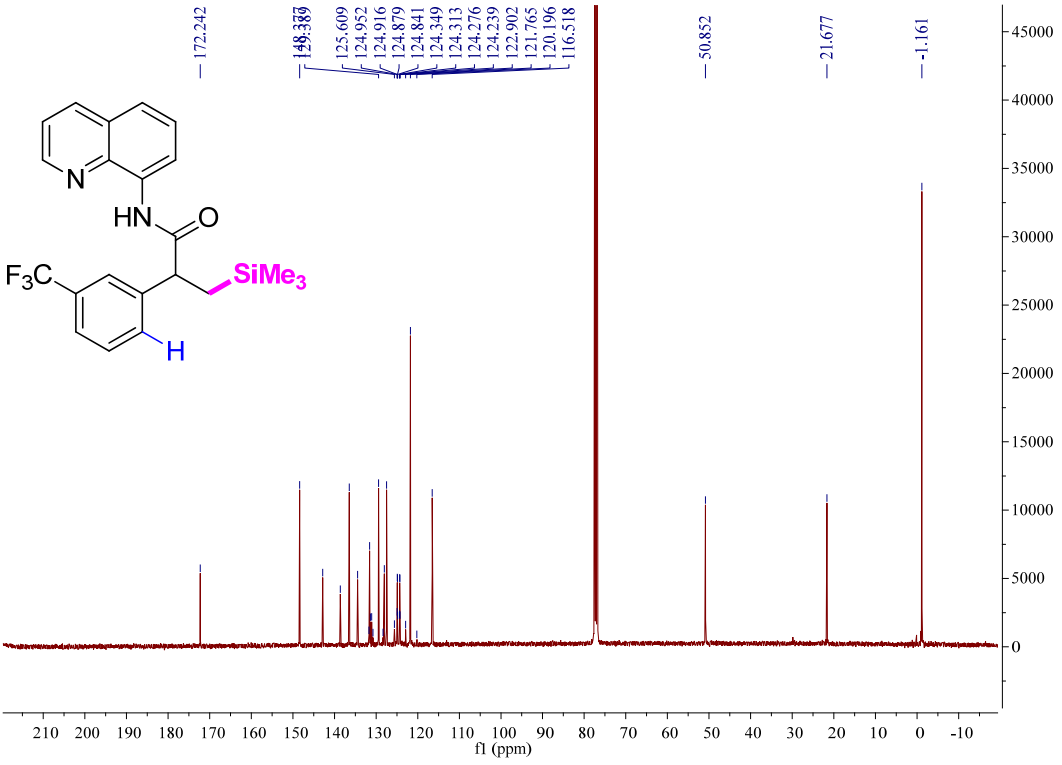
9.05
f1 (ppm)
N
HN
O
F3C
SiMe3
H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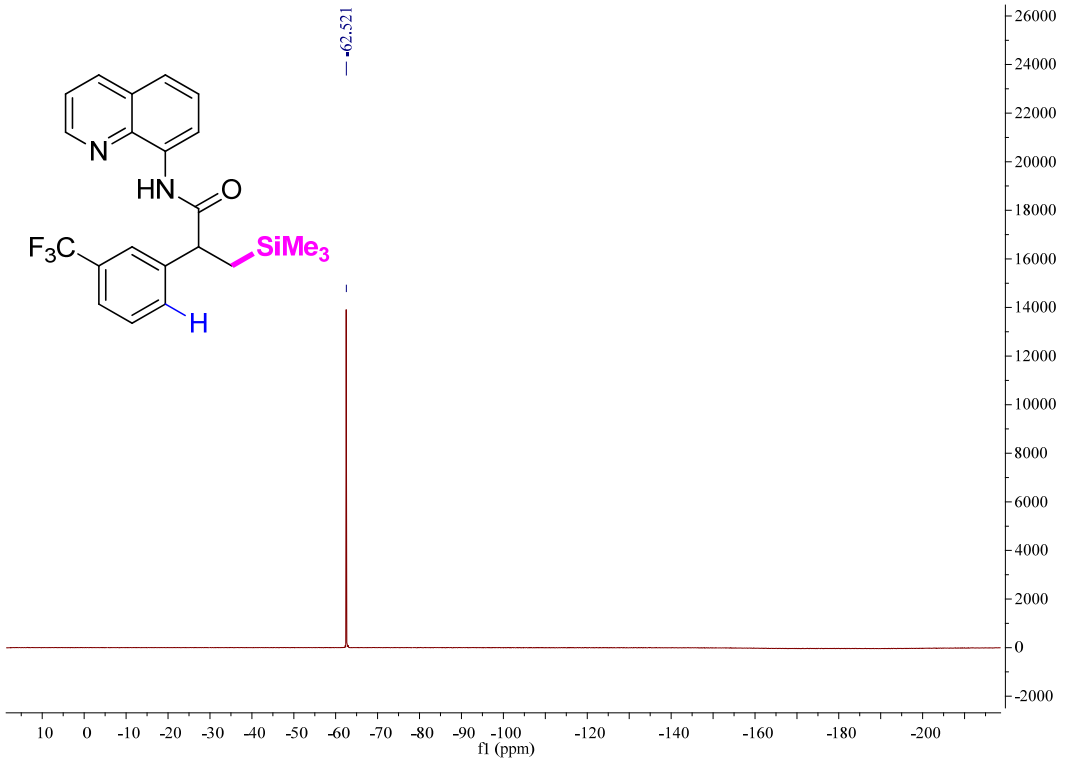
HN
O
F3C
SiMe3
H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N
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H
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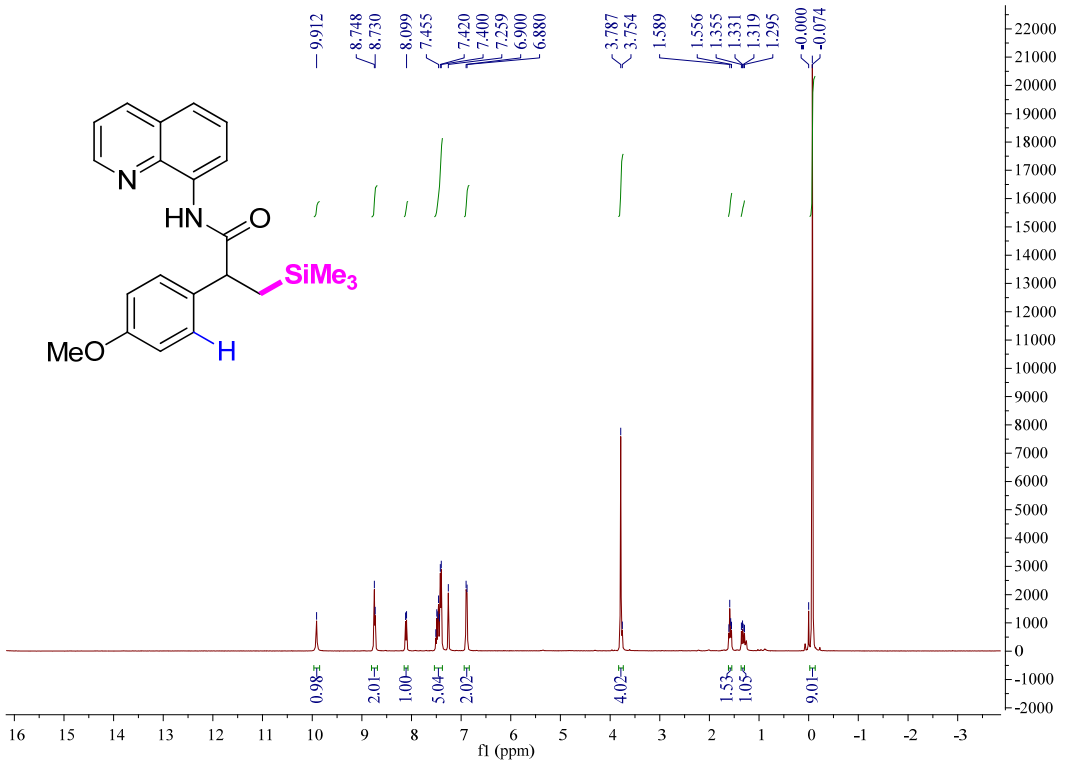
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

6h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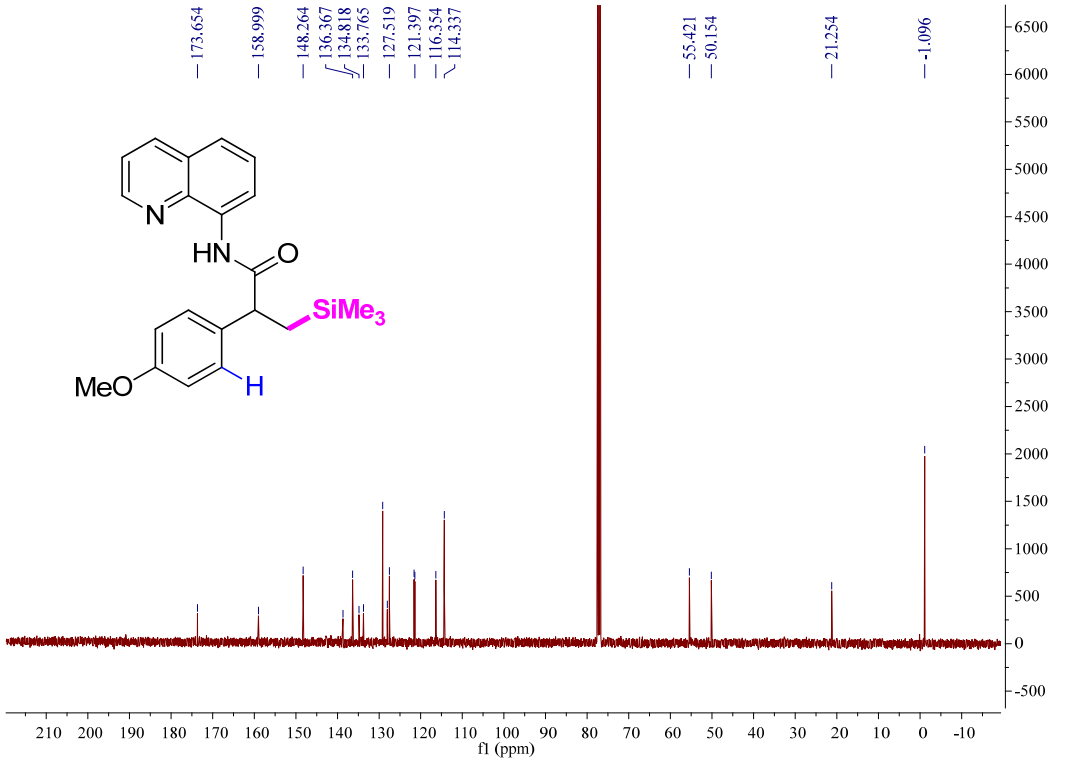
7.420
7.400
7.259
6.900
6.880
3.787
3.754
1.589
1.556
1.355
1.331
1.319
1.295
0.000
-0.074
0.98
2.01
1.00
5.04
2.02
4.02
1.53
1.05
9.01
N
HN
O
SiMe3
MeO
H
f1 (ppm)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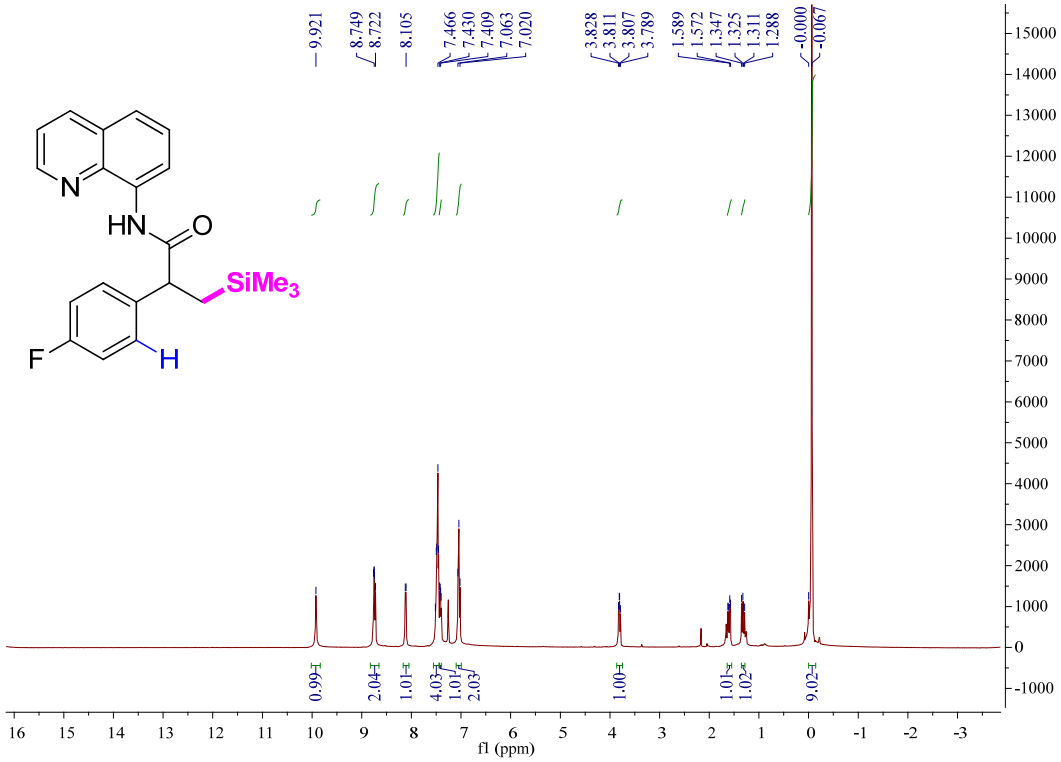
148.264
136.367
134.818
133.765
127.519
121.397
116.354
114.337
55.421
50.154
21.254
-1.096
N
HN
O
SiMe3
MeO
H
f1 (ppm)

6i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8.749
8.722
8.105
7.466
7.430
7.409
7.063
7.020
3.828
3.811
3.807
3.789
1.589
1.572
1.347
1.325
1.311
1.288
-0.000
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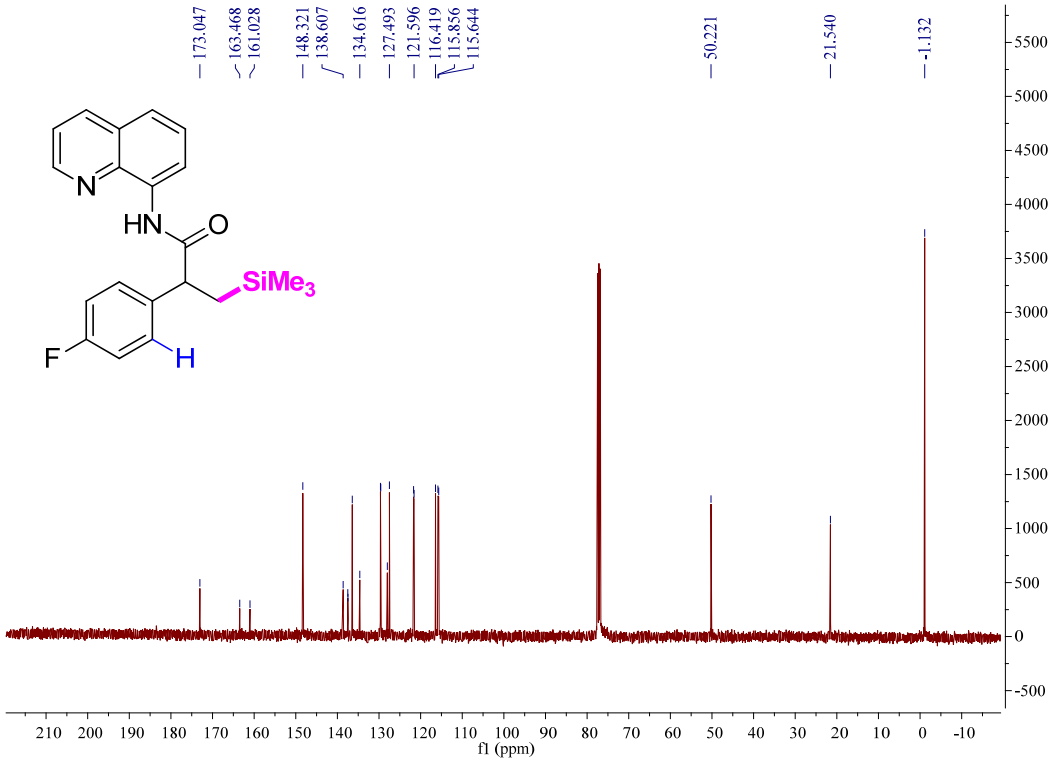
2.04
1.01
4.03
1.01
2.03
1.00
1.01
1.02
9.02
f1 (ppm)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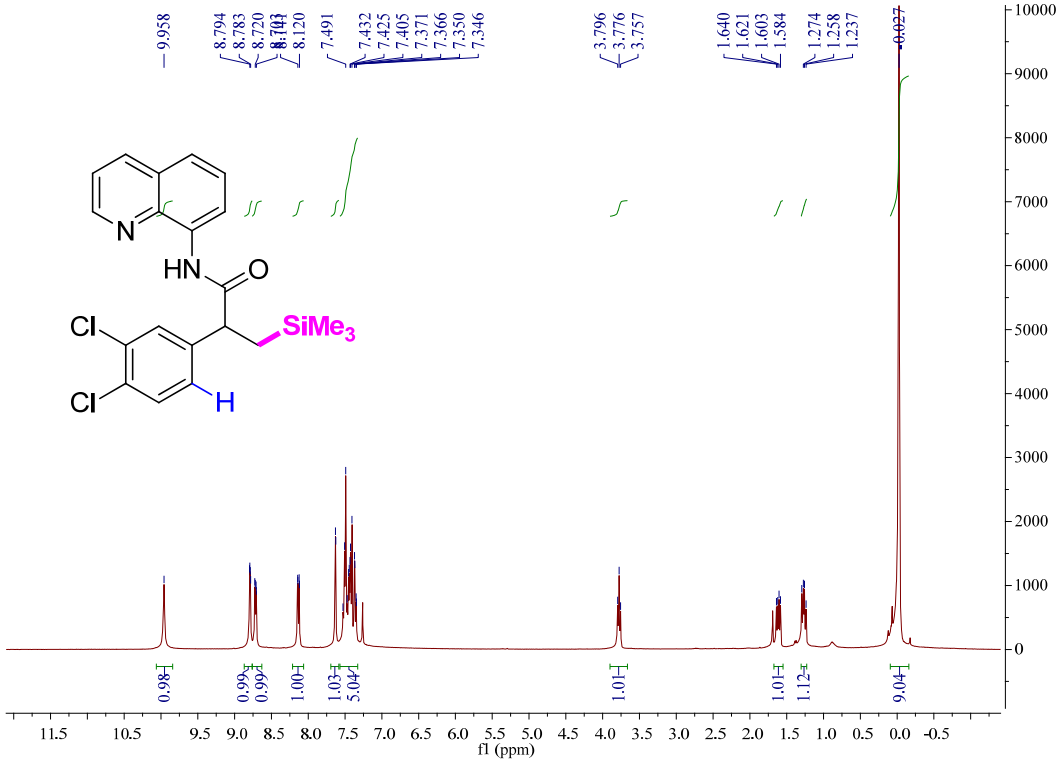
163.468
161.028
148.321
138.607
134.616
127.493
121.596
116.419
115.856
115.644
50.221
21.540
-1.132
f1 (ppm)

6l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8.794
8.783
8.720
8.710
8.120
7.491
7.432
7.425
7.405
7.371
7.366
7.350
7.346
3.796
3.776
3.757
1.640
1.621
1.603
1.584
1.274
1.258
1.237
0.027
N
HN
O
Cl
Cl
SiMe3
H
0.98
0.99
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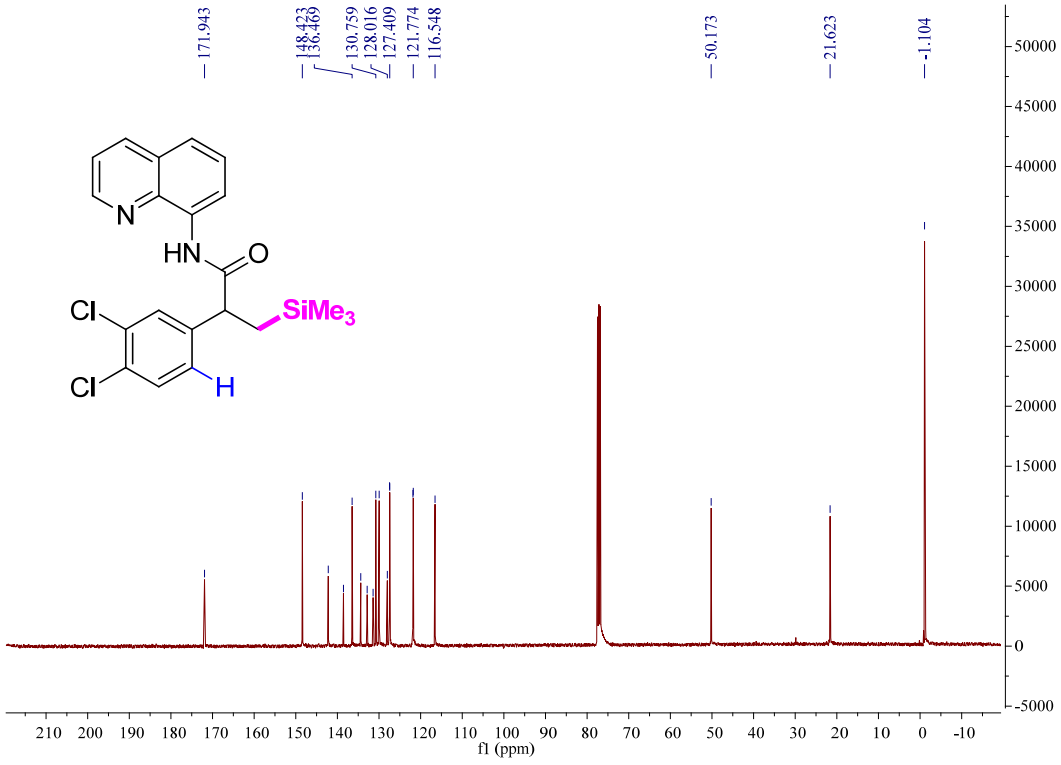
1.00
1.03
5.04
1.01
1.01
1.12
9.04
f1 (ppm)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136.469
130.759
128.016
127.409
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116.548
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21.623
-1.104
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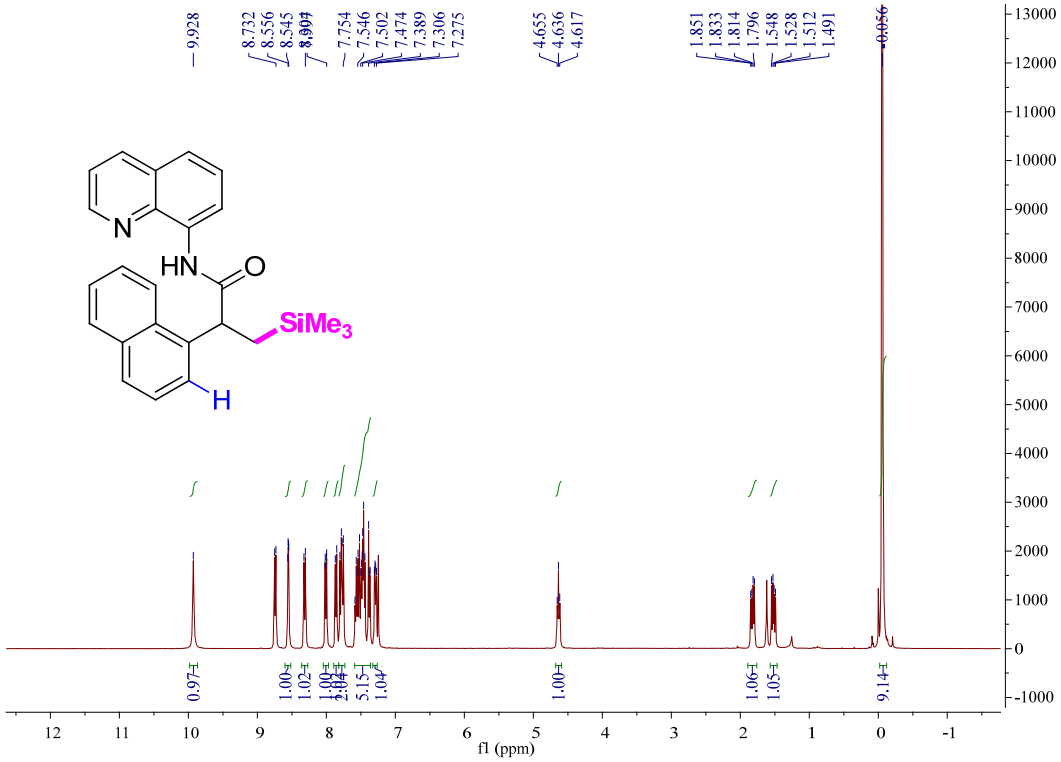
HN
O
Cl
Cl
SiMe3
H
f1 (ppm)

6j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8.732
8.556
8.545
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7.546
7.502
7.474
7.389
7.306
7.275
4.655
4.636
4.617
1.851
1.833
1.814
1.796
1.548
1.528
1.512
1.491
0.056
0.97
1.00
1.02
1.00
2.04
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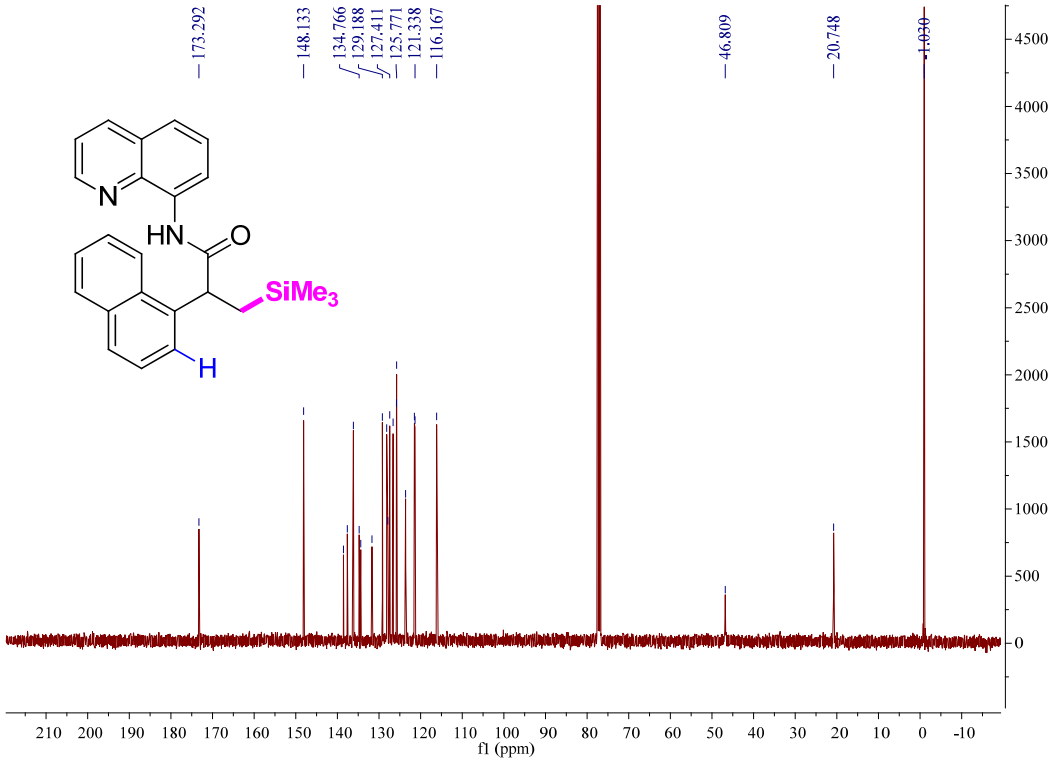
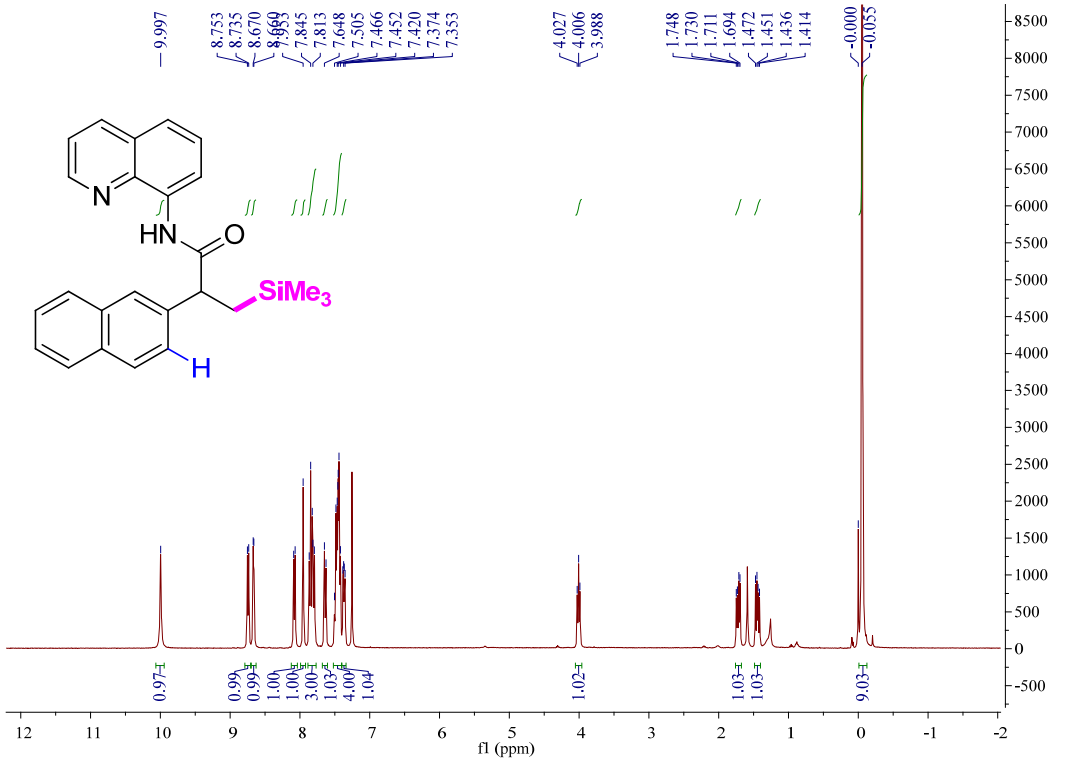
1.04
1.00
1.06
1.05
9.14
HN
O
SiMe3
H
f1 (ppm)


173.292
148.133
134.766
129.188
127.411
125.771
121.338
116.167
46.809
20.748
1.030
HN
O
SiMe3
H
f1 (ppm)

6k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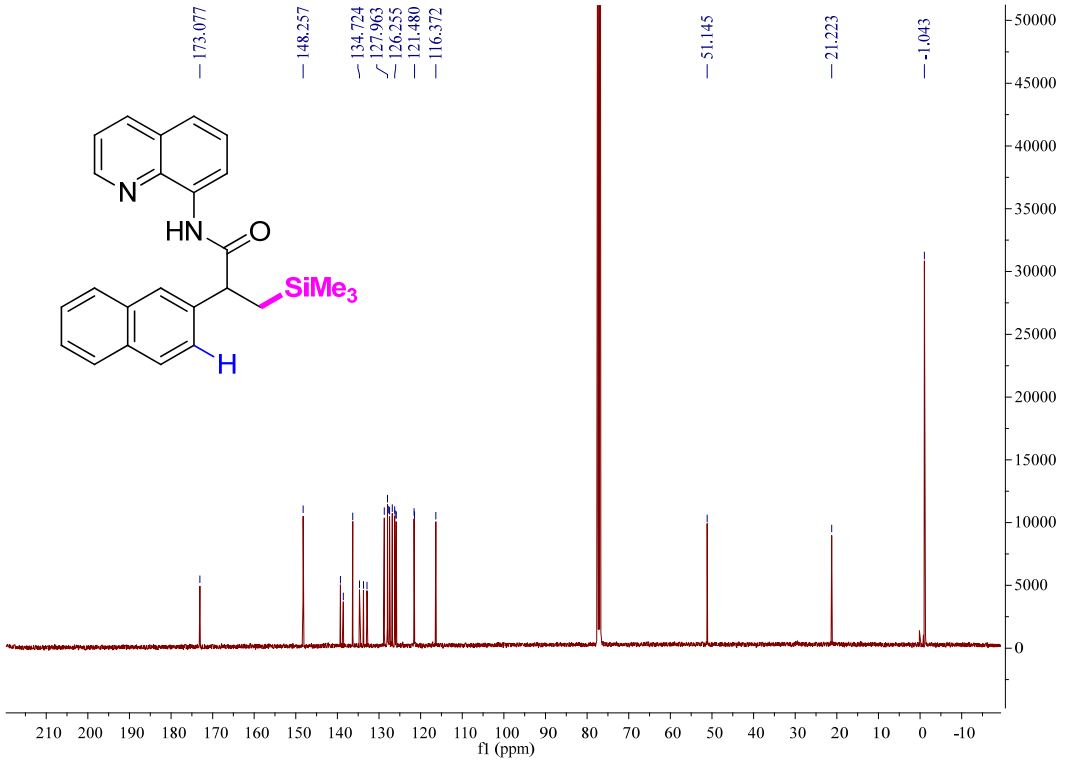
8.753
8.735
8.670
8.660
7.845
7.813
7.648
7.505
7.466
7.452
7.420
7.374
7.353
4.027
4.006
3.988
1.748
1.730
1.711
1.694
1.472
1.451
1.436
1.414
0.000
-0.055
N
HN
O
SiMe3
H
0.97
0.99
0.99
1.00
1.00
3.00
1.03
4.00
1.04
1.02
1.03
1.03
9.03
f1 (ppm)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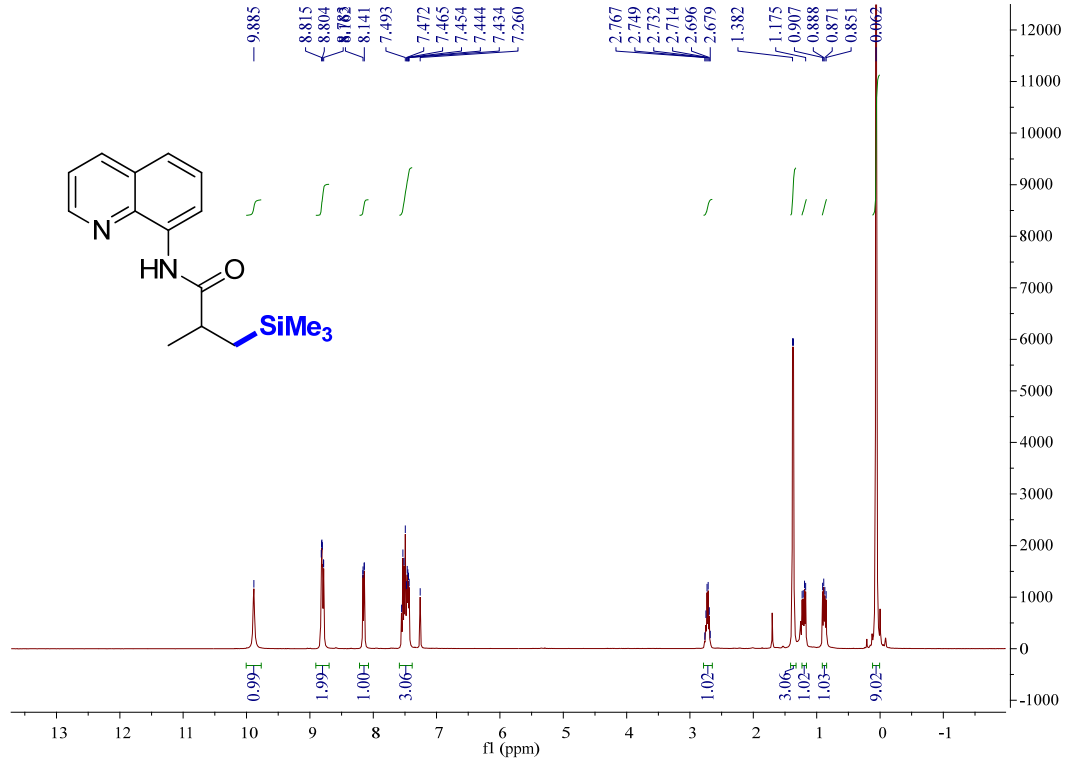
148.257
134.724
127.963
126.255
121.480
116.372
51.145
21.223
-1.043
N
HN
O
SiMe3
H
f1 (ppm)

6m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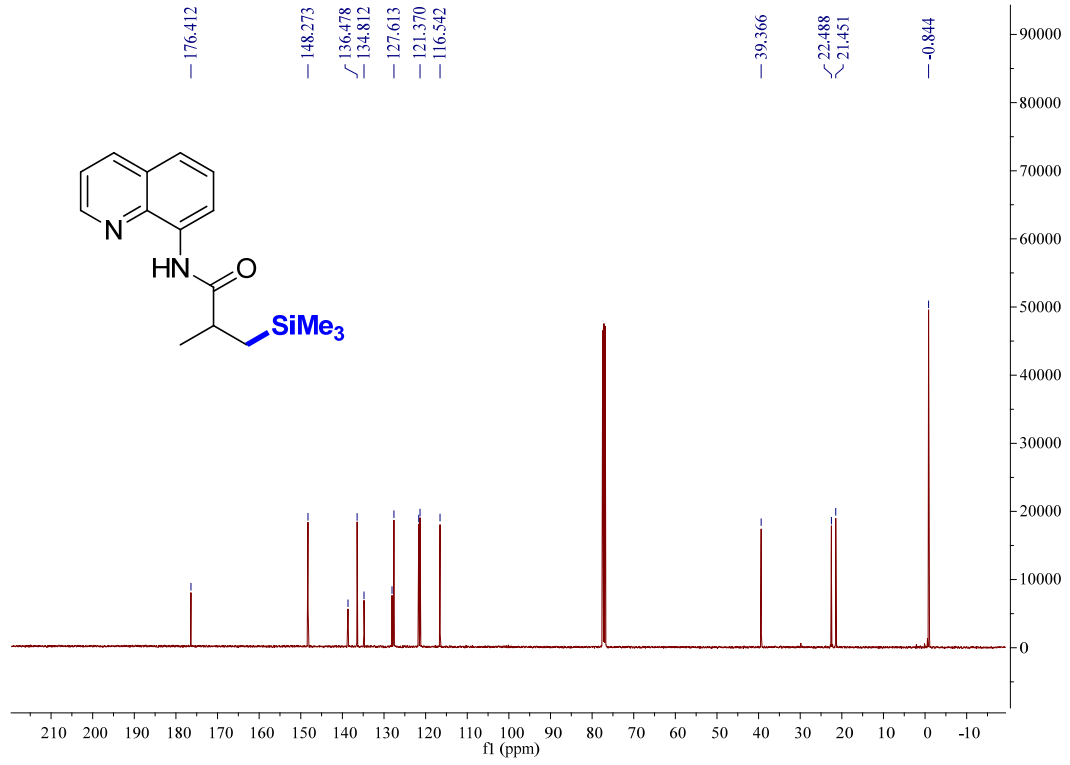
8.815
8.804
8.141
7.493
7.472
7.465
7.454
7.444
7.434
7.260
2.767
2.749
2.732
2.714
2.696
2.679
1.382
1.175
0.907
0.888
0.871
0.851
0.062
0.99
1.99
1.00
3.06
1.02
3.06
1.02
1.03
9.02
HN
O
SiMe3
f1 (ppm)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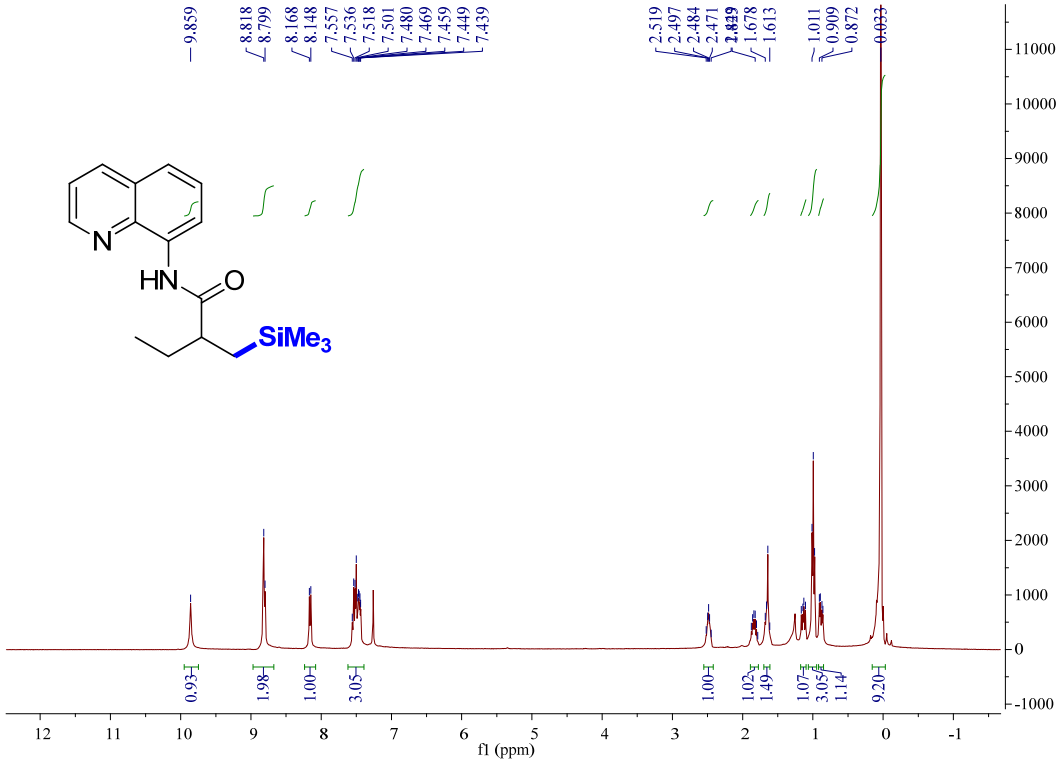
148.273
136.478
134.812
127.613
121.370
116.542
39.366
22.488
21.451
-0.844
HN
O
SiMe3
f1 (ppm)

6n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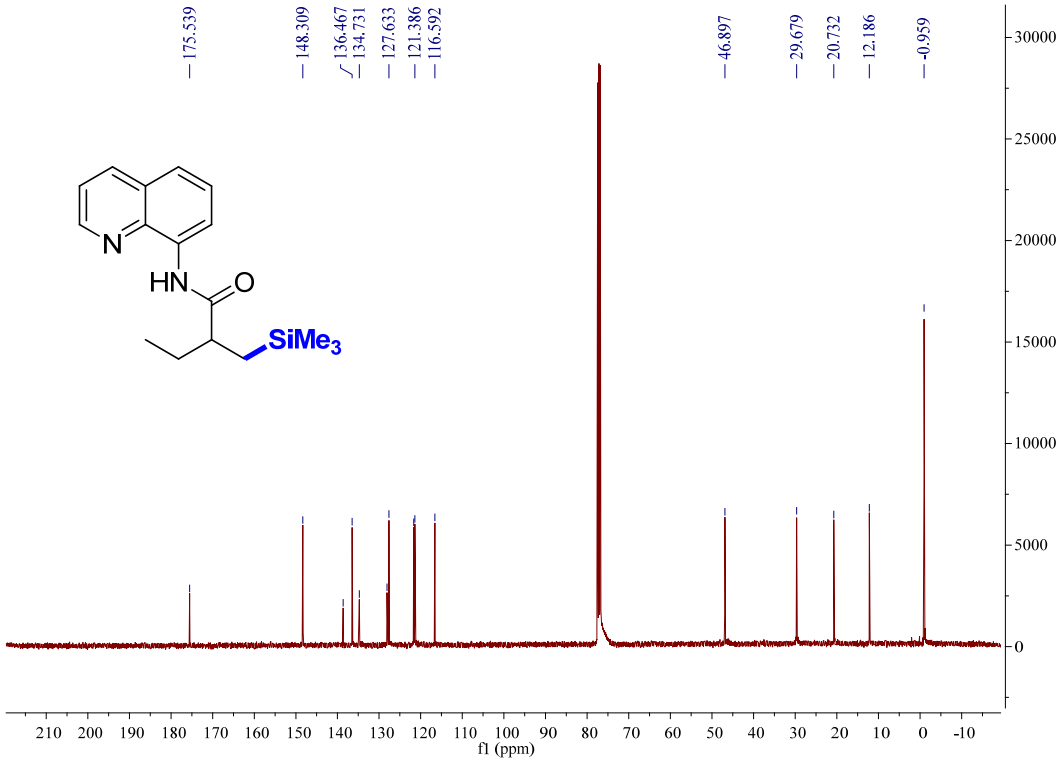
8.818
8.799
8.168
8.148
7.557
7.536
7.518
7.501
7.480
7.469
7.459
7.449
7.439
2.519
2.497
2.484
2.471
1.678
1.613
1.011
0.909
0.872
0.033
N
HN
O
SiMe3
0.93
1.98
1.00
3.05
1.00
1.02
1.49
1.07
3.05
1.14
9.20
f1 (ppm)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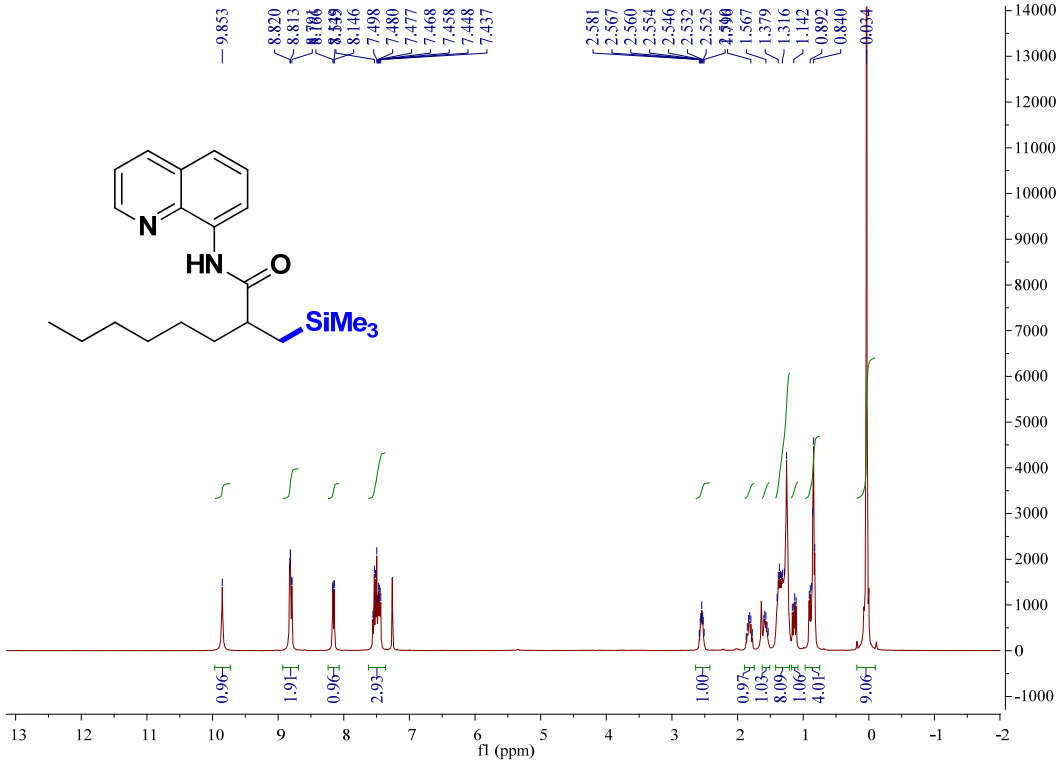
148.309
136.467
134.731
127.633
121.386
116.592
46.897
29.679
20.732
12.186
-0.959
N
HN
O
SiMe3
f1 (ppm)

6o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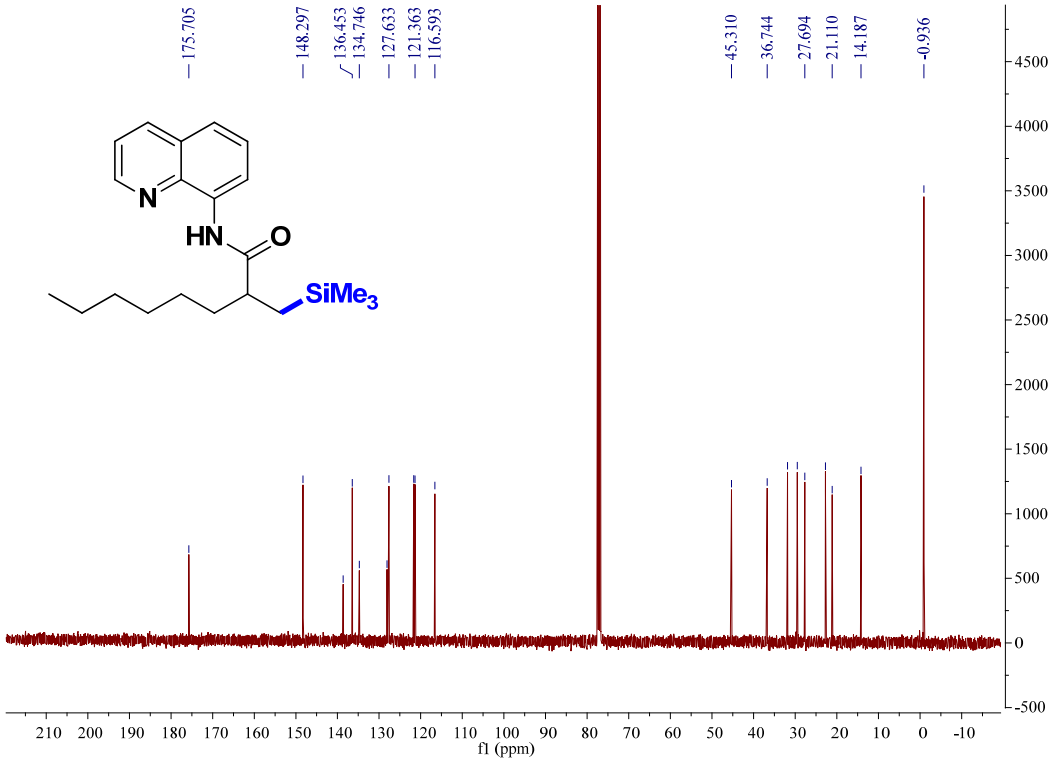
8.820
8.813
8.146
7.498
7.480
7.477
7.468
7.458
7.448
7.437
2.581
2.567
2.560
2.554
2.546
2.532
2.525
1.567
1.379
1.316
1.142
0.892
0.840
0.034
0.96
1.91
0.96
2.93
1.00
0.97
1.03
8.09
1.06
4.01
9.06
HN
O
SiMe3
f1 (ppm)


175.705
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136.453
134.746
127.633
121.363
116.593
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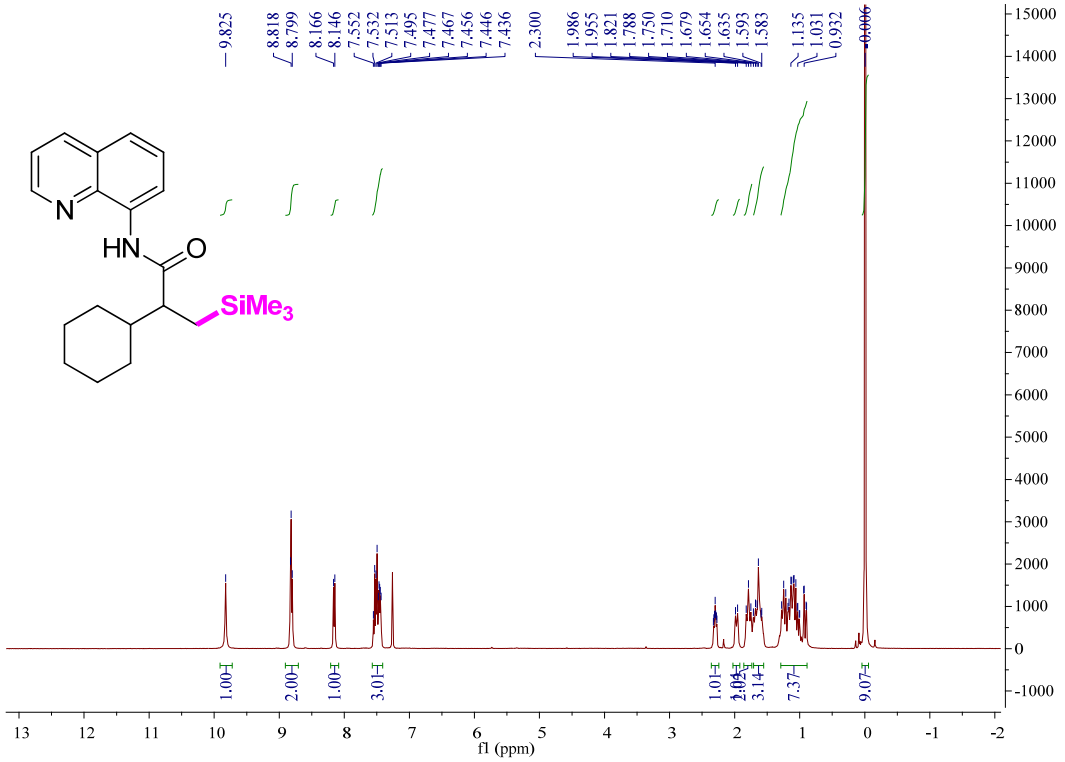
27.694
21.110
14.187
-0.936
HN
O
SiMe3
f1 (ppm)

6p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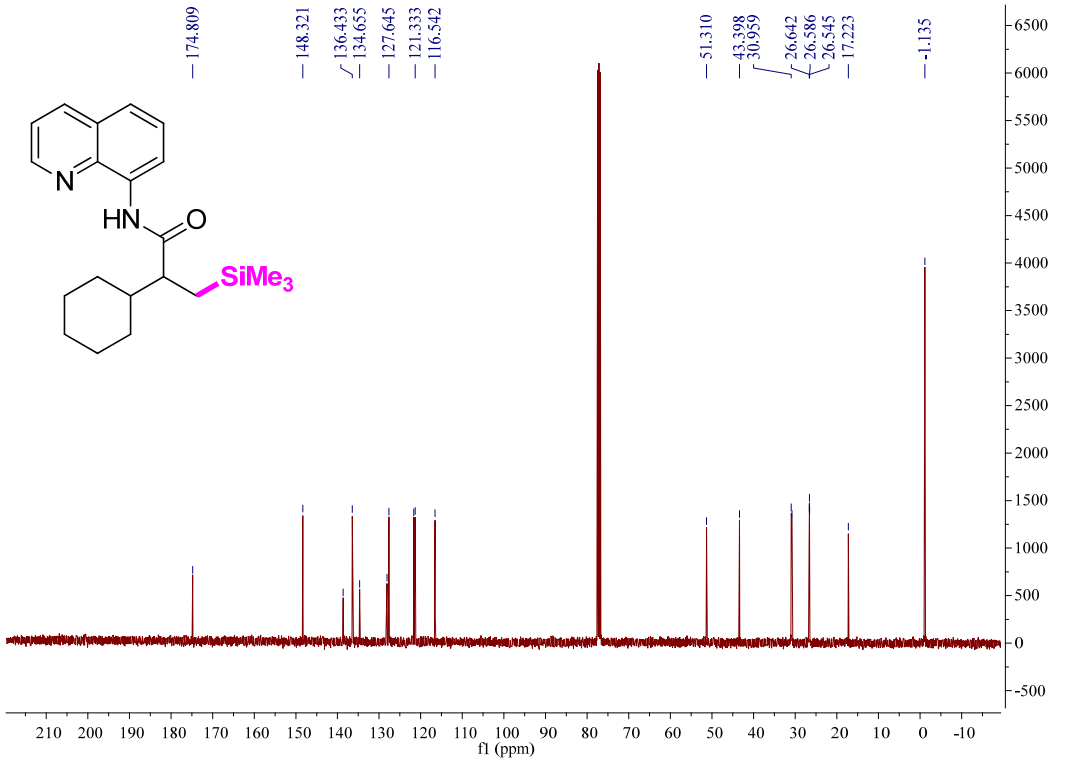
8.799
8.166
8.146
7.552
7.532
7.513
7.495
7.477
7.467
7.456
7.446
7.436
2.300
1.986
1.955
1.821
1.788
1.750
1.710
1.679
1.654
1.635
1.593
1.583
1.135
1.031
0.932
0.000
1.00
2.00
1.00
3.01
1.01
3.14
7.37
9.07
f1 (ppm)
HN
O
SiMe3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136.433
134.655
127.645
121.333
116.542
51.310
43.398
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26.642
26.586
26.545
17.223
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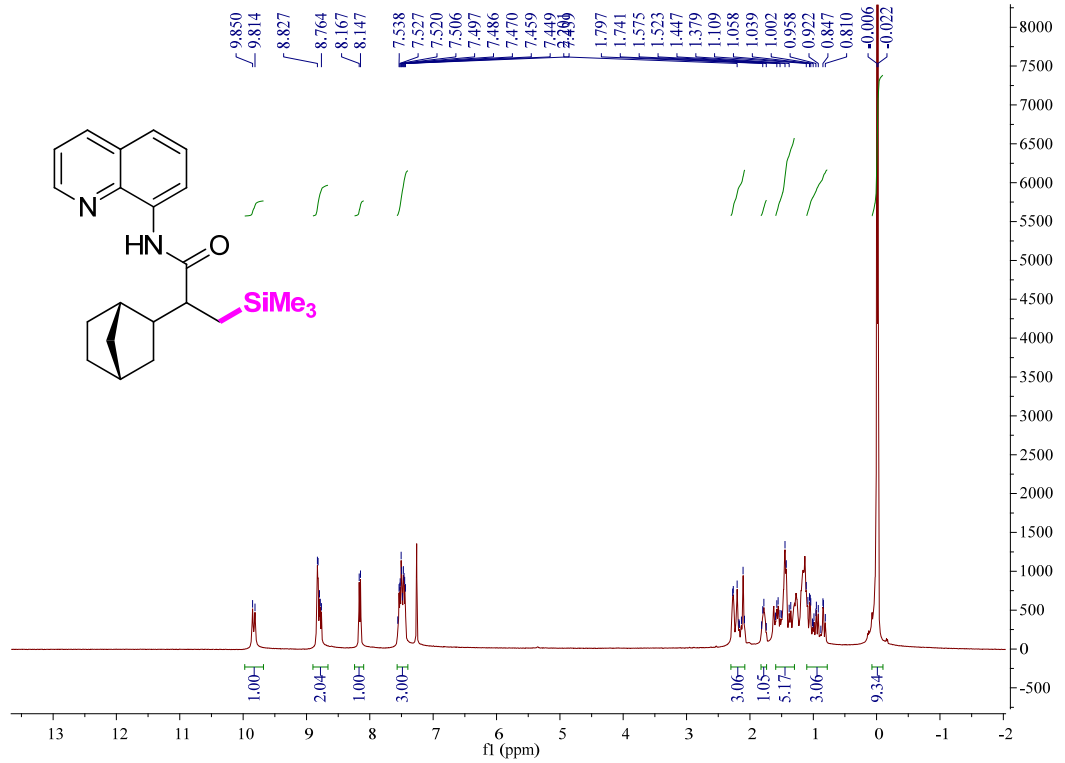
f1 (ppm)
HN
O
SiMe3

6q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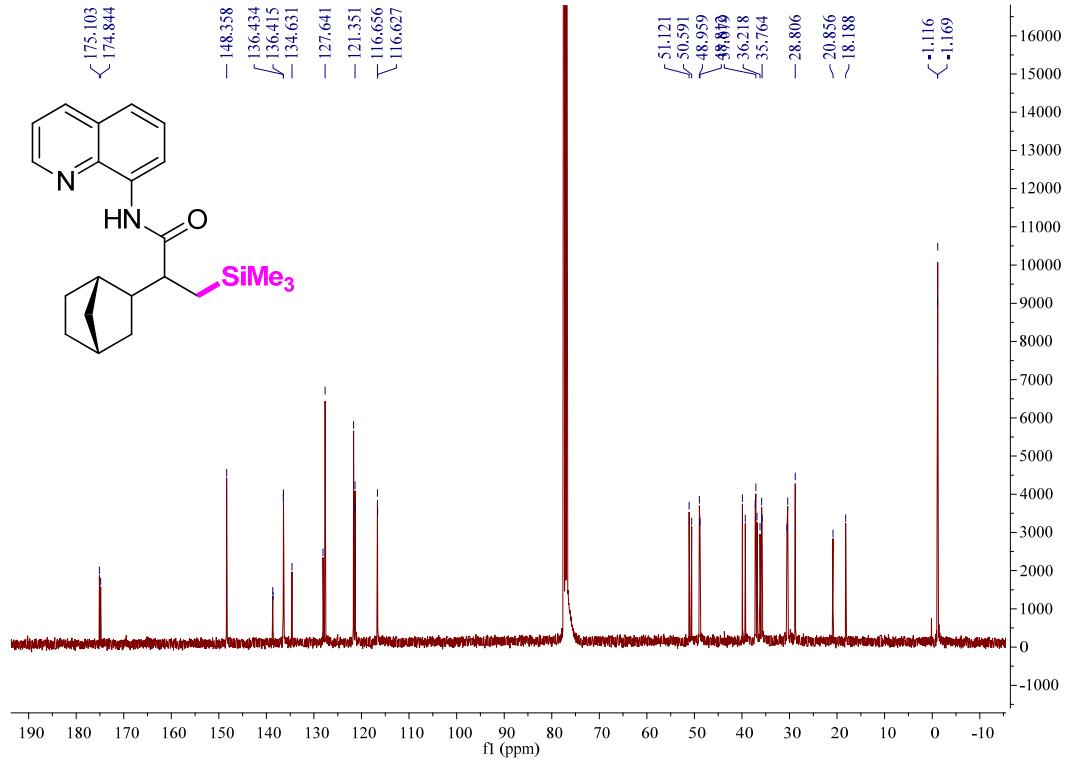
9.814
8.827
8.764
8.167
8.147
7.538
7.527
7.520
7.506
7.497
7.486
7.470
7.459
7.449
1.797
1.741
1.575
1.523
1.447
1.379
1.109
1.058
1.039
1.002
0.958
0.922
0.847
0.810
-0.006
-0.022
HN
O
SiMe3
1.00
2.04
1.00
3.00
3.06
1.05
5.17
3.06
9.34
f1 (ppm)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136.415
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127.641
121.351
116.656
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51.121
50.591
48.959
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28.806
20.856
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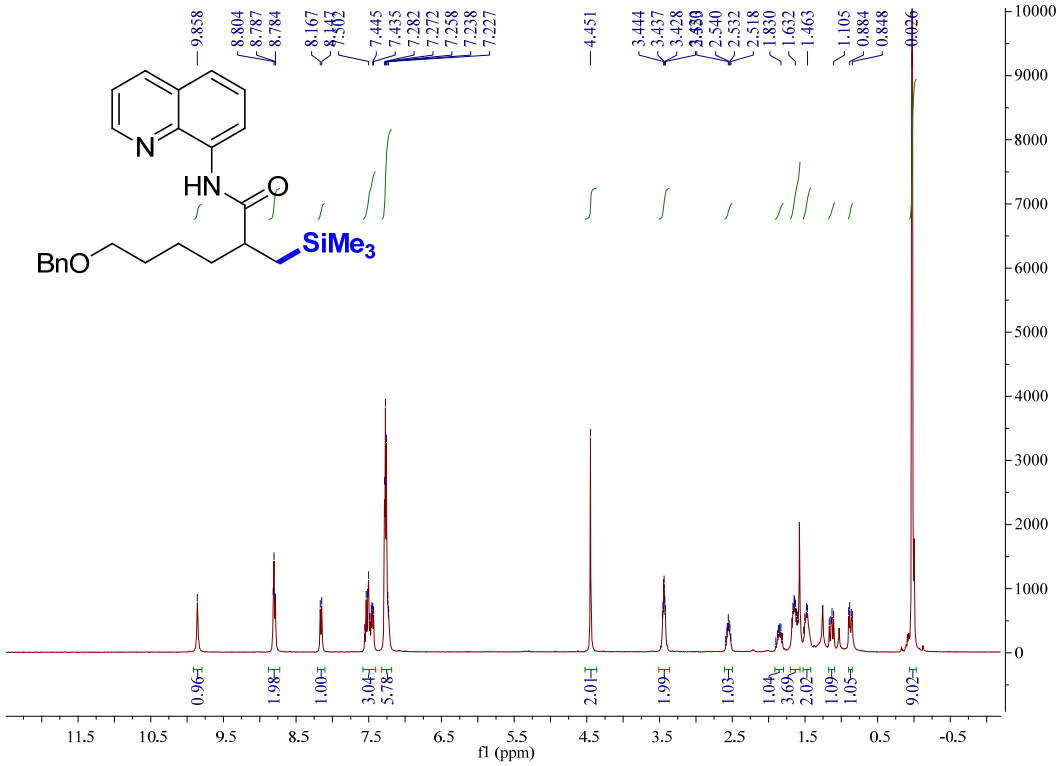
-1.169
HN
O
SiMe3
f1 (ppm)

6r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8.784
8.167
8.147
7.502
7.445
7.435
7.282
7.272
7.258
7.238
7.227
4.451
3.444
3.437
3.428
2.540
2.532
2.518
1.830
1.632
1.463
1.105
0.884
0.848
0.026
HN
O
BnO
SiMe3
0.96
1.98
1.00
3.04
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1.99
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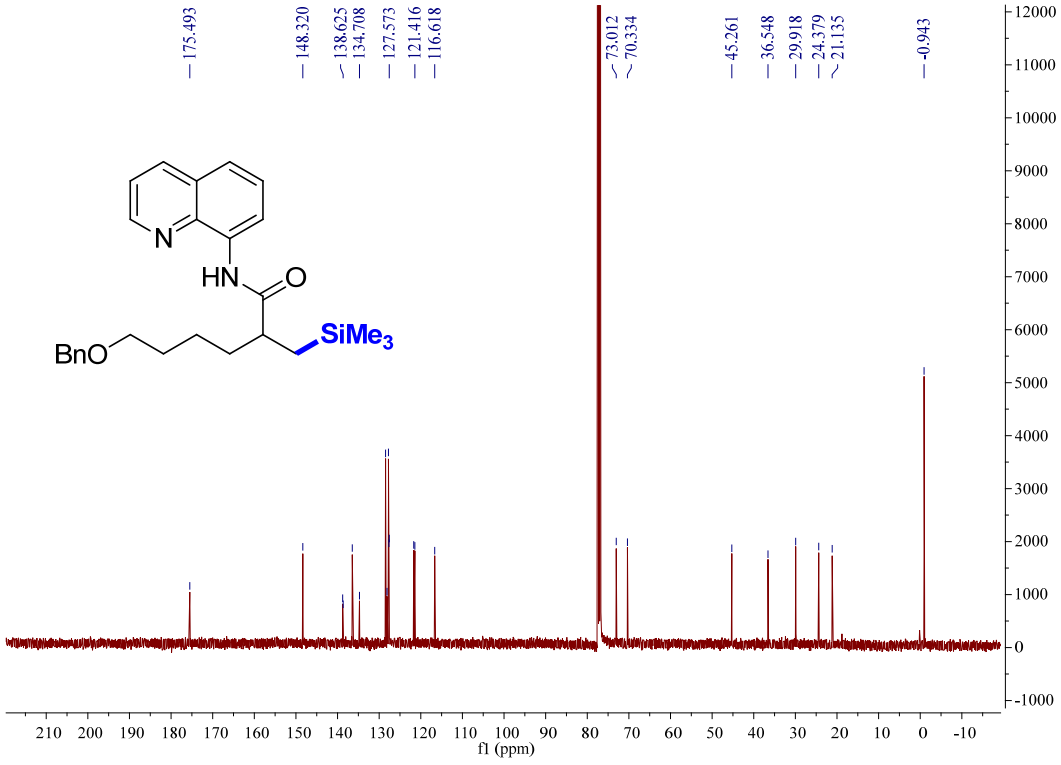
2.02
1.09
1.05
9.02
f1 (ppm)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73.012
70.334
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36.548
29.918
24.379
21.135
0.943
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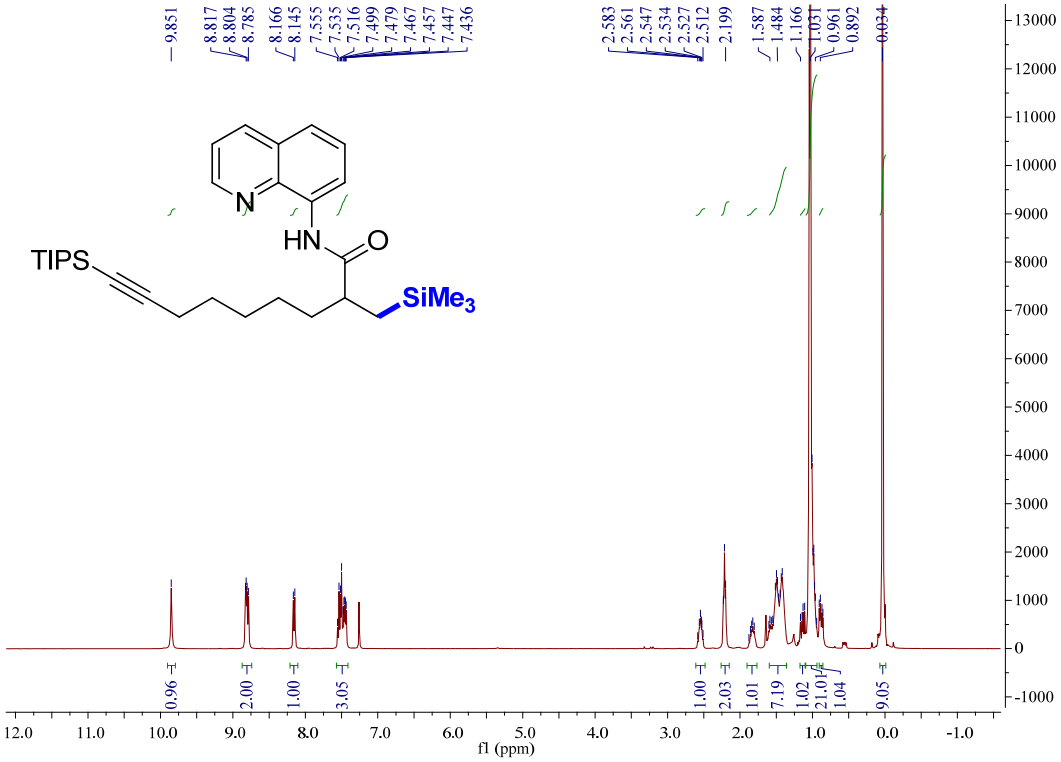
O
BnO
SiMe3
f1 (ppm)

6s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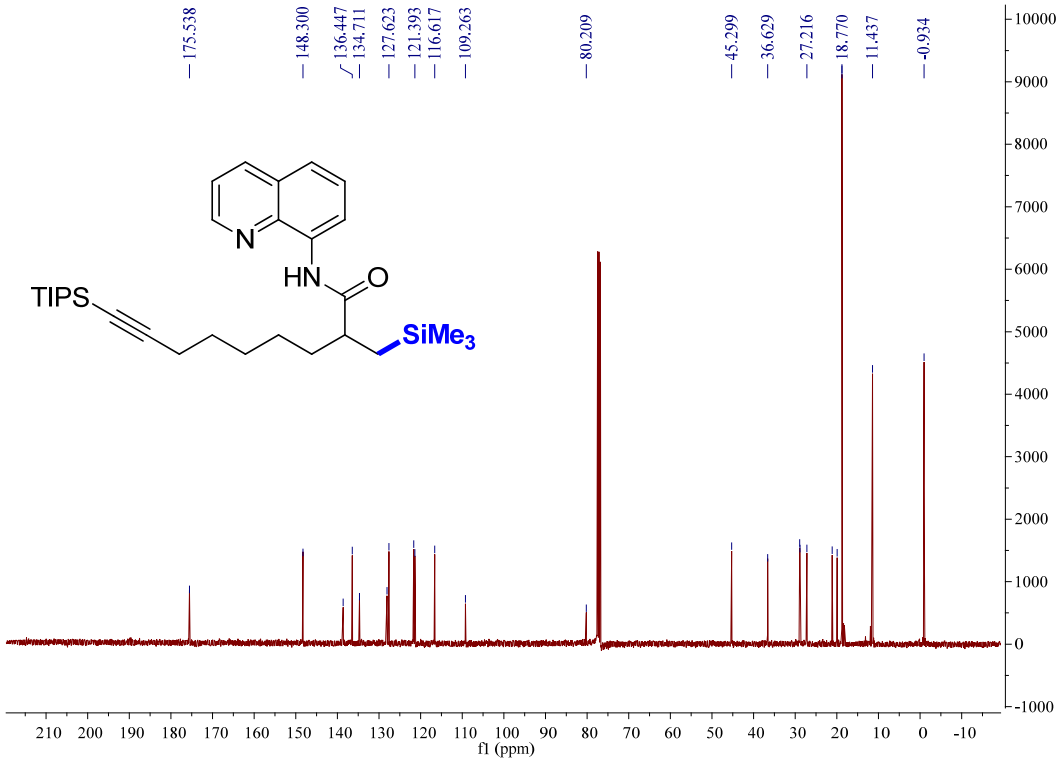
8.804
8.785
8.166
8.145
7.555
7.535
7.516
7.499
7.479
7.467
7.457
7.447
7.436
2.583
2.561
2.547
2.534
2.527
2.512
2.199
1.587
1.484
1.166
1.031
0.961
0.892
0.034
TIPS
HN
O
N
SiMe3
f1 (ppm)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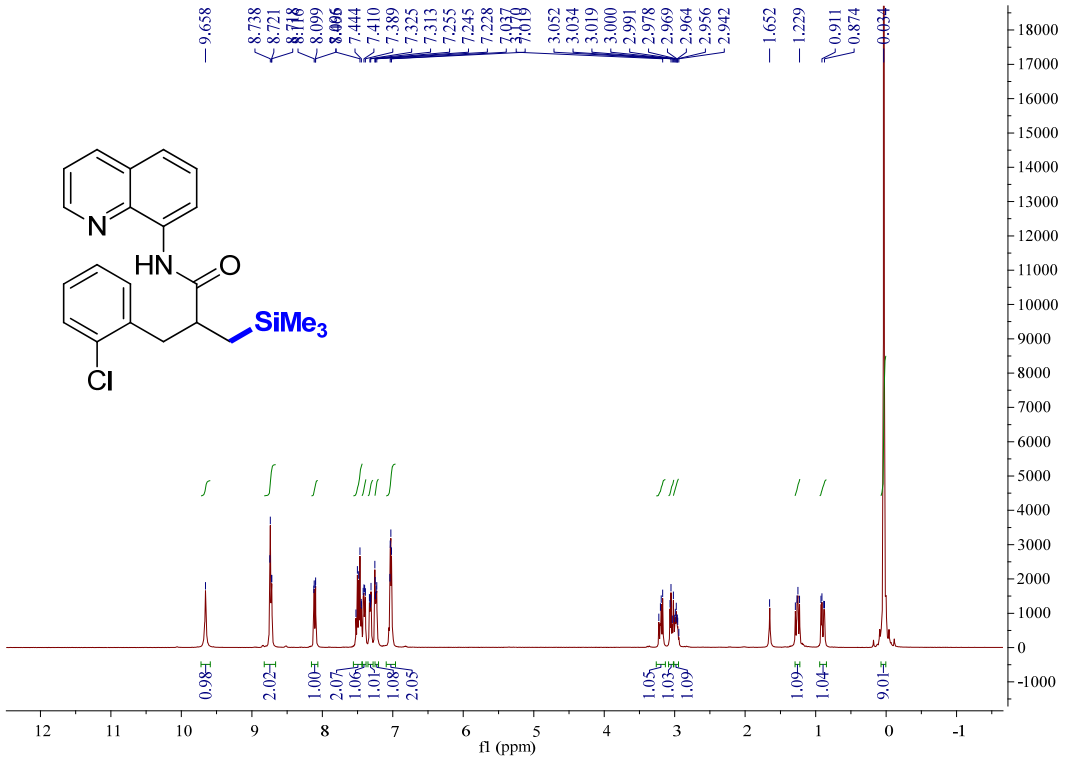
134.711
127.623
121.393
116.617
109.263
80.209
45.299
36.629
27.216
18.770
11.437
-0.934
TIPS
HN
O
N
SiMe3
f1 (ppm)

6t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8.099
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7.410
7.389
7.325
7.313
7.255
7.245
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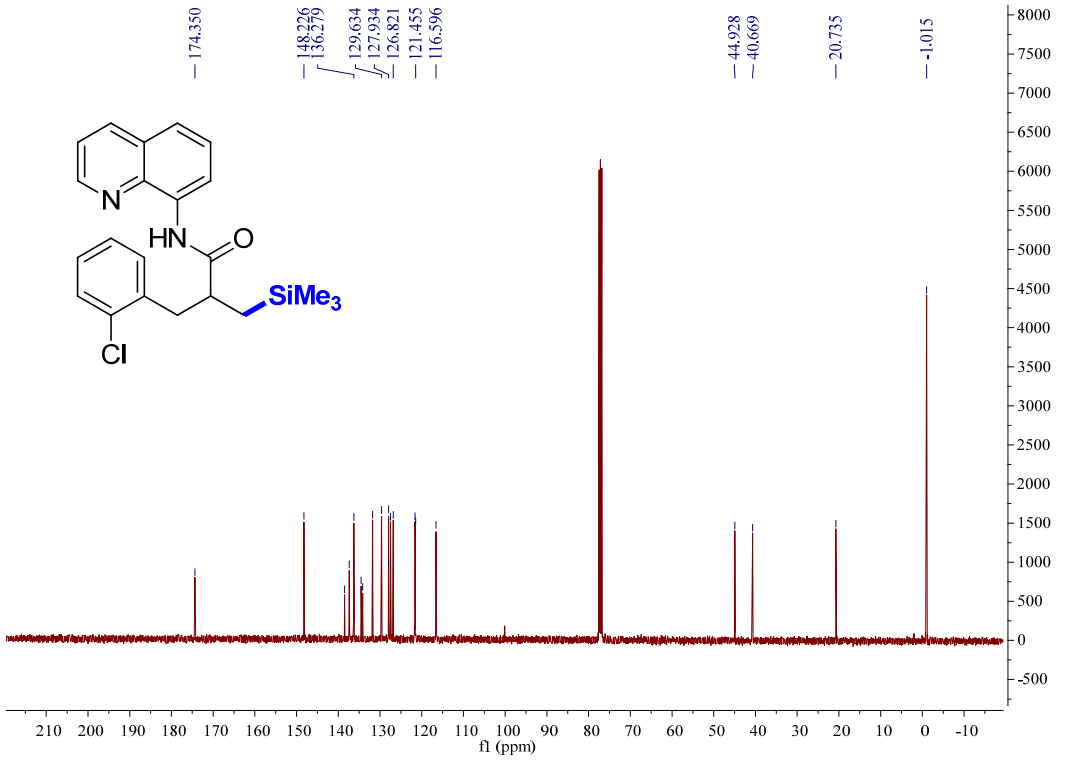
3.034
3.019
3.000
2.991
2.978
2.969
2.964
2.956
2.942
1.652
1.229
0.911
0.874
0.034
0.98
2.02
1.00
2.07
1.06
1.01
1.08
2.05
1.05
1.03
1.09
1.09
1.04
9.01
HN
O
SiMe3
Cl
f1 (ppm)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127.934
126.821
121.455
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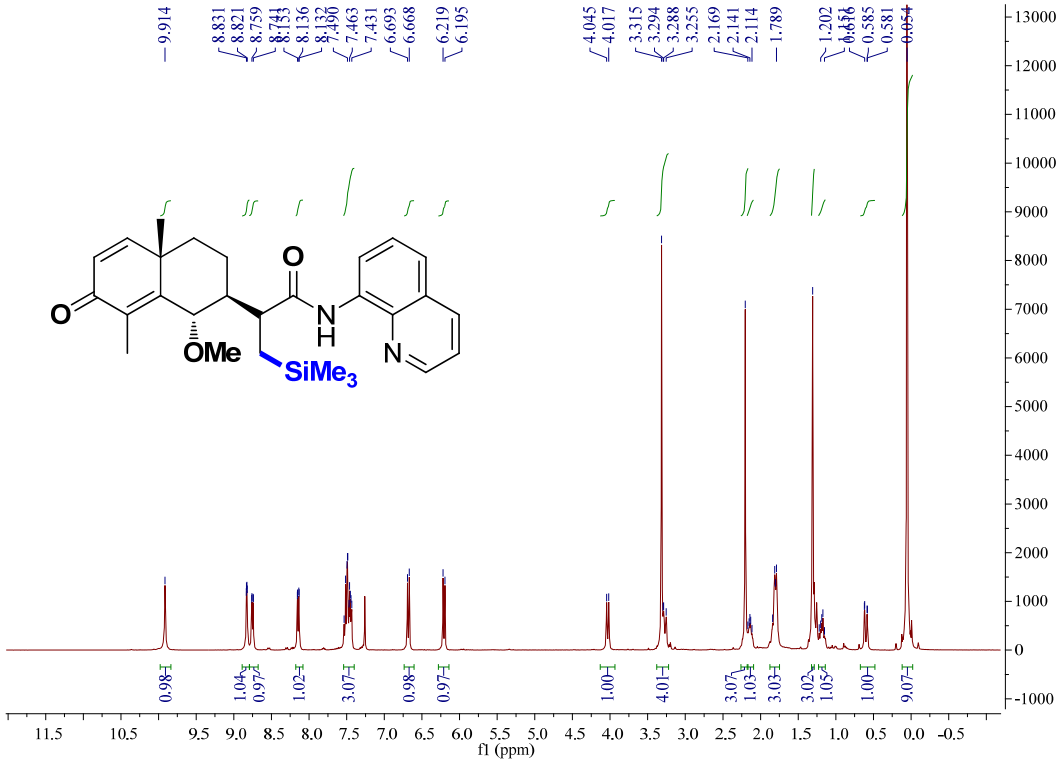
44.928
40.669
20.735
-1.015
HN
O
SiMe3
Cl
f1 (ppm)

6u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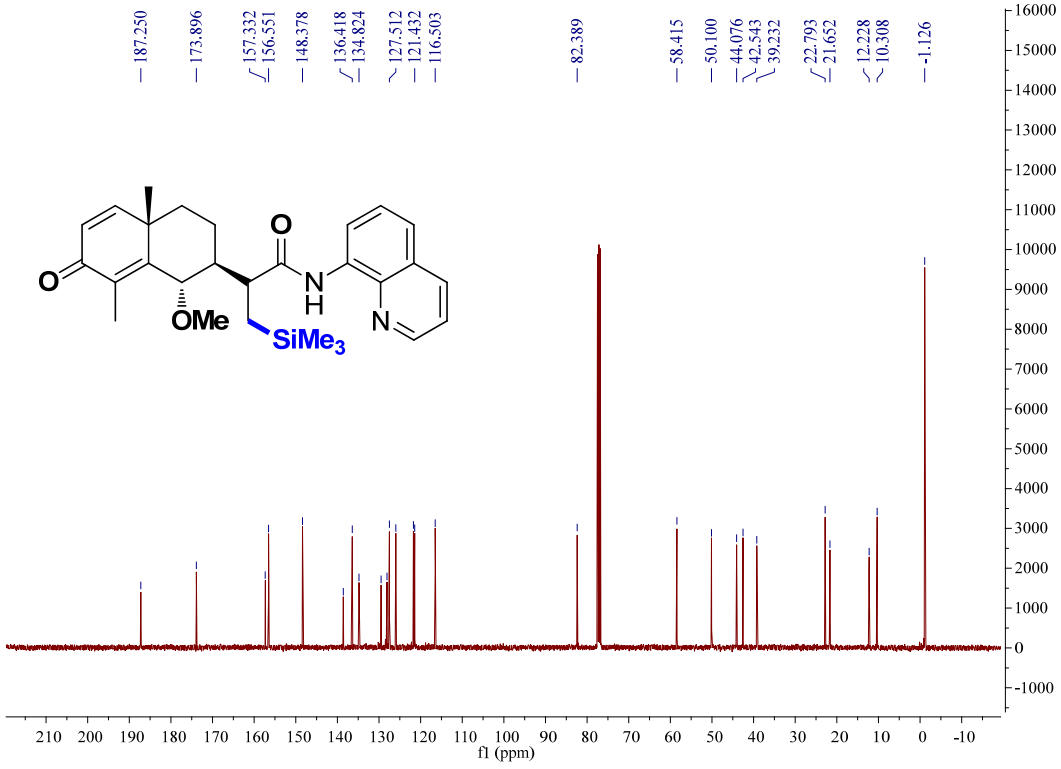
8.759
8.743
8.136
8.132
7.490
7.463
7.431
6.693
6.668
6.219
6.195
4.045
4.017
3.315
3.294
3.288
3.255
2.169
2.141
2.114
1.789
1.202
0.585
0.581
0.054
O
N
H
OMe
SiMe3
f1 (ppm)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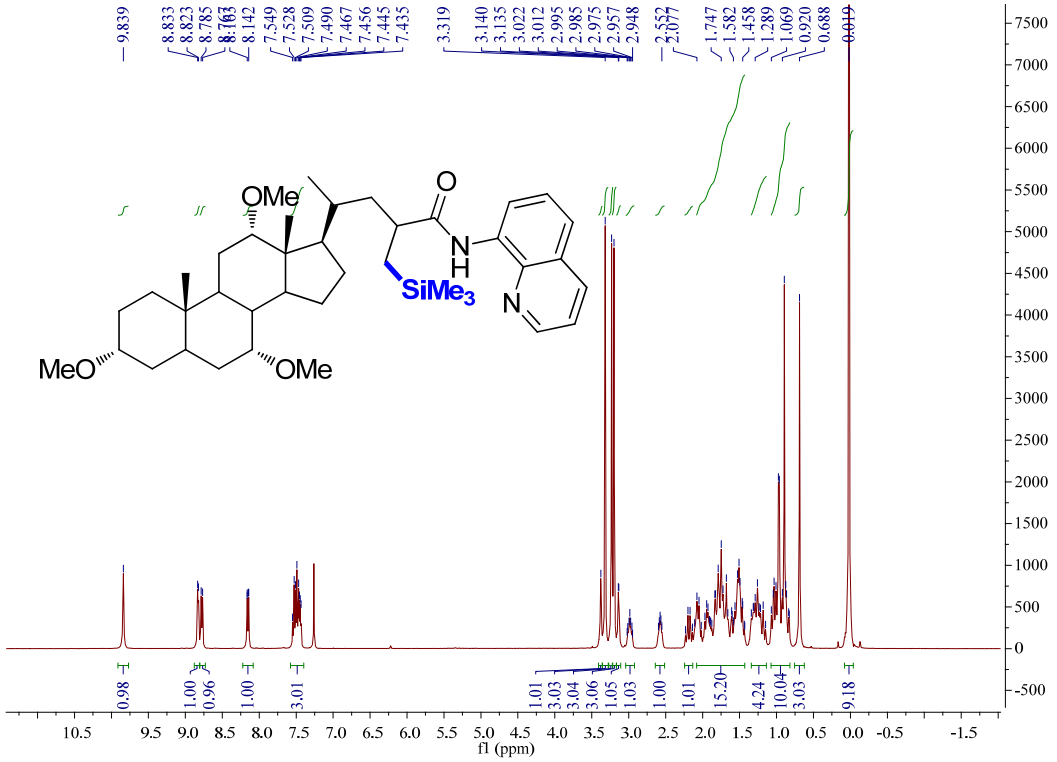
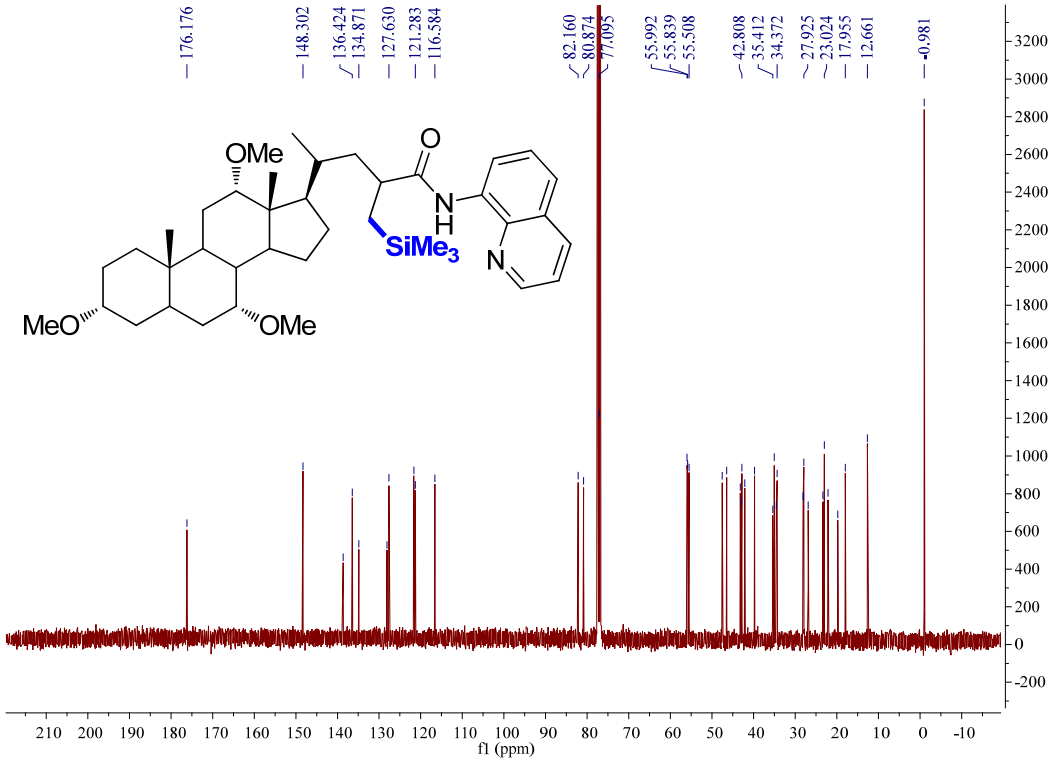
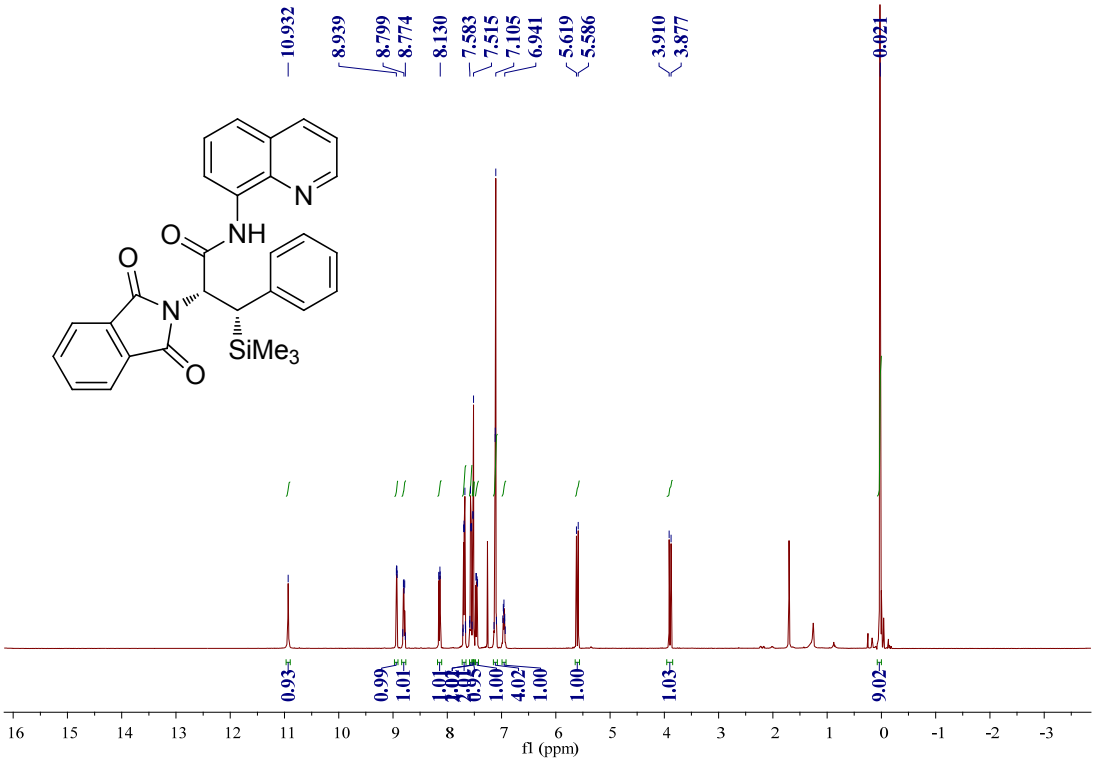
173.896
157.332
156.551
148.378
136.418
134.824
127.512
121.432
116.503
82.389
58.415
50.100
44.076
42.543
39.232
22.793
21.652
12.228
10.308
-1.126
O
N
H
OMe
SiMe3
f1 (ppm)

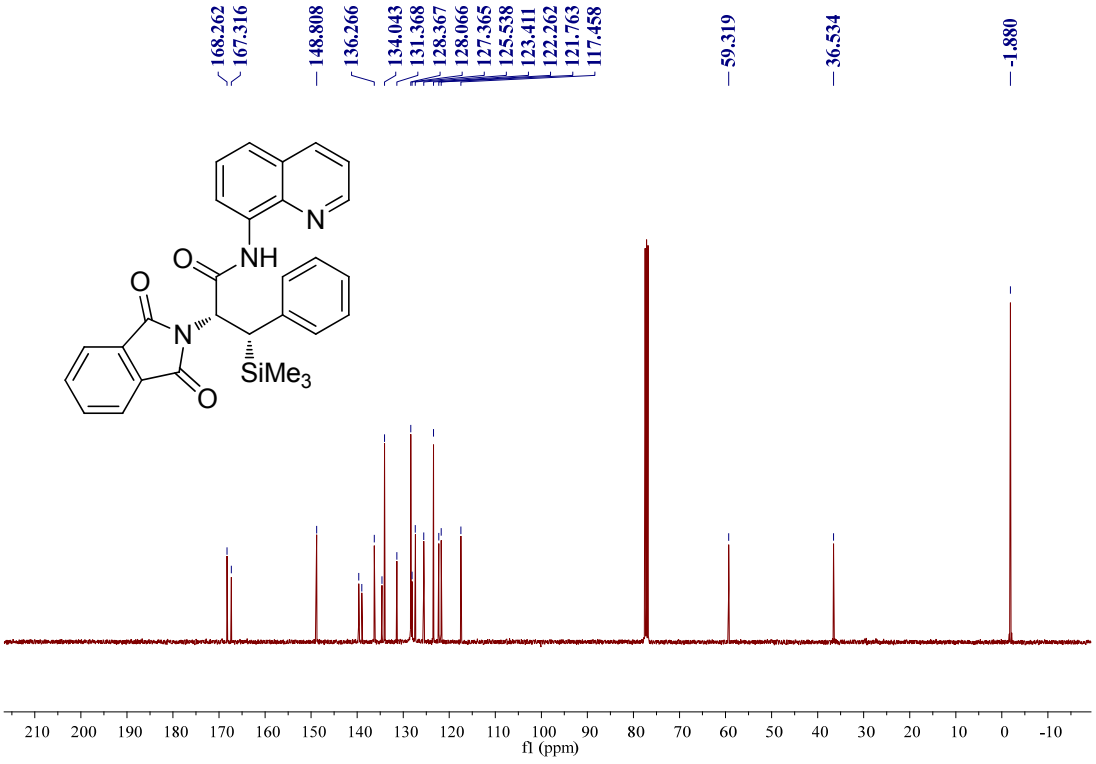
6v


9.839
8.833
8.823
8.785
8.142
7.549
7.528
7.509
7.490
7.467
7.456
7.445
7.435
3.319
3.140
3.135
3.022
3.012
2.995
2.985
2.975
2.957
2.948
2.552
2.077
1.747
1.582
1.458
1.289
1.069
0.920
0.688
0.019
OMe
O
N
H
SiMe3
N
MeO
OMe
0.98
1.00
0.96
1.00
3.01
1.01
3.03
3.04
3.06
1.05
1.03
1.00
1.01
15.20
4.24
10.04
3.03
9.18
f1 (ppm)

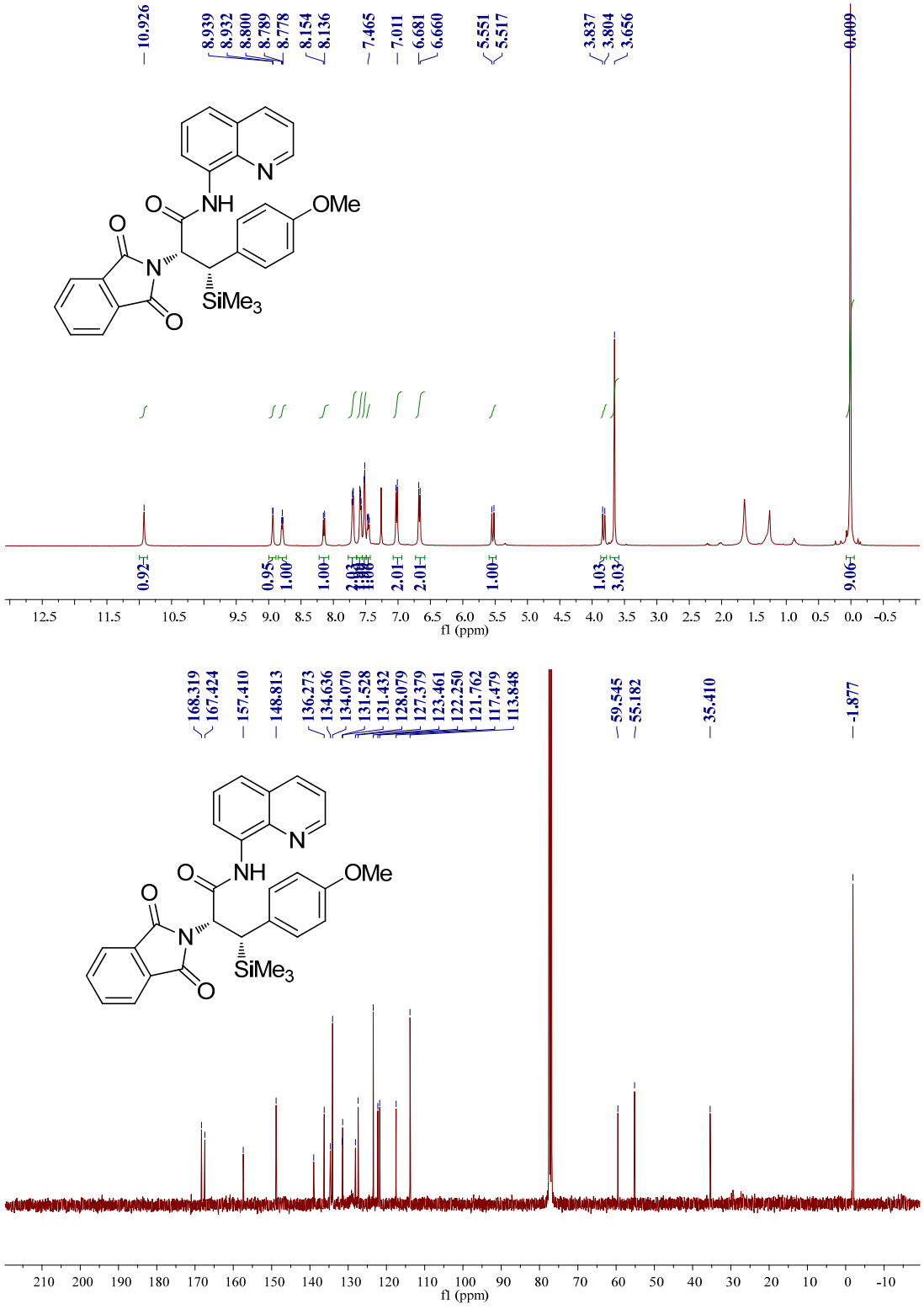

176.176
148.302
136.424
134.871
127.630
121.283
116.584
82.160
80.874
77.095
55.992
55.839
55.508
42.808
35.412
34.372
27.925
23.024
17.955
12.661
0.981
OMe
O
N
H
SiMe3
N
MeO
OMe
f1 (ppm)

3a

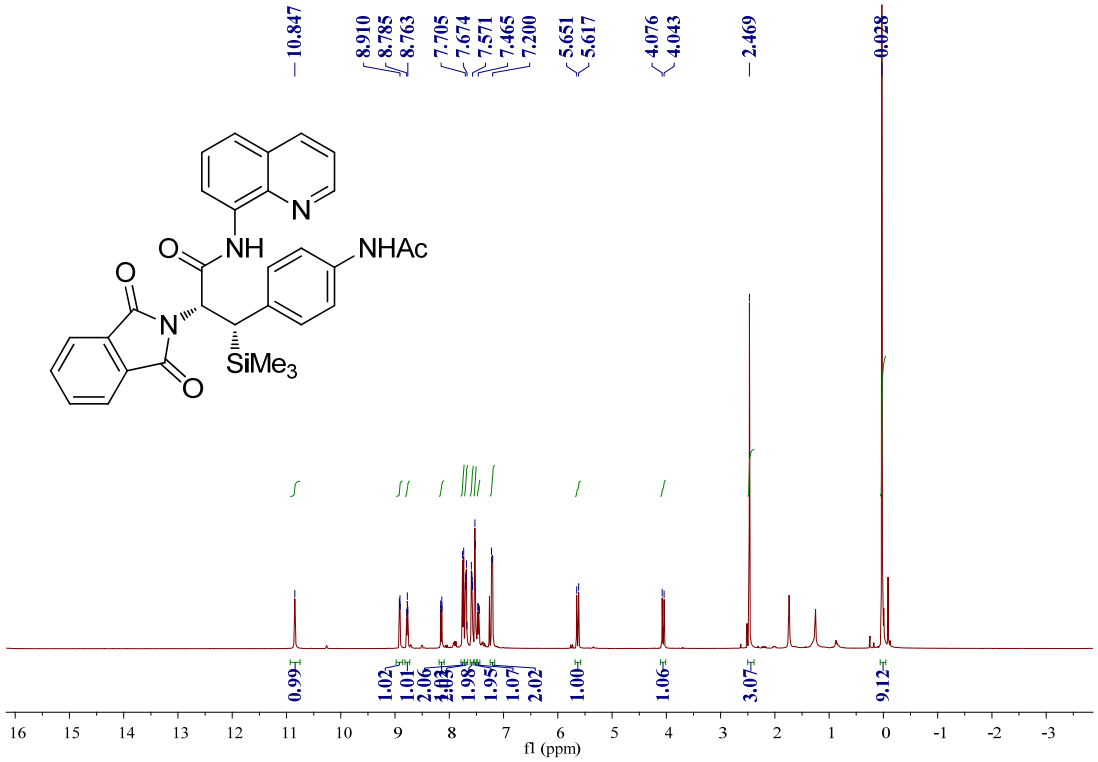

10.932
8.939
8.799
8.774
8.130
7.583
7.515
7.105
6.941
5.619
5.586
3.910
3.877
0.021
0.93
0.99
1.01
1.00
4.02
1.00
1.00
1.03
9.02
f1 (ppm)

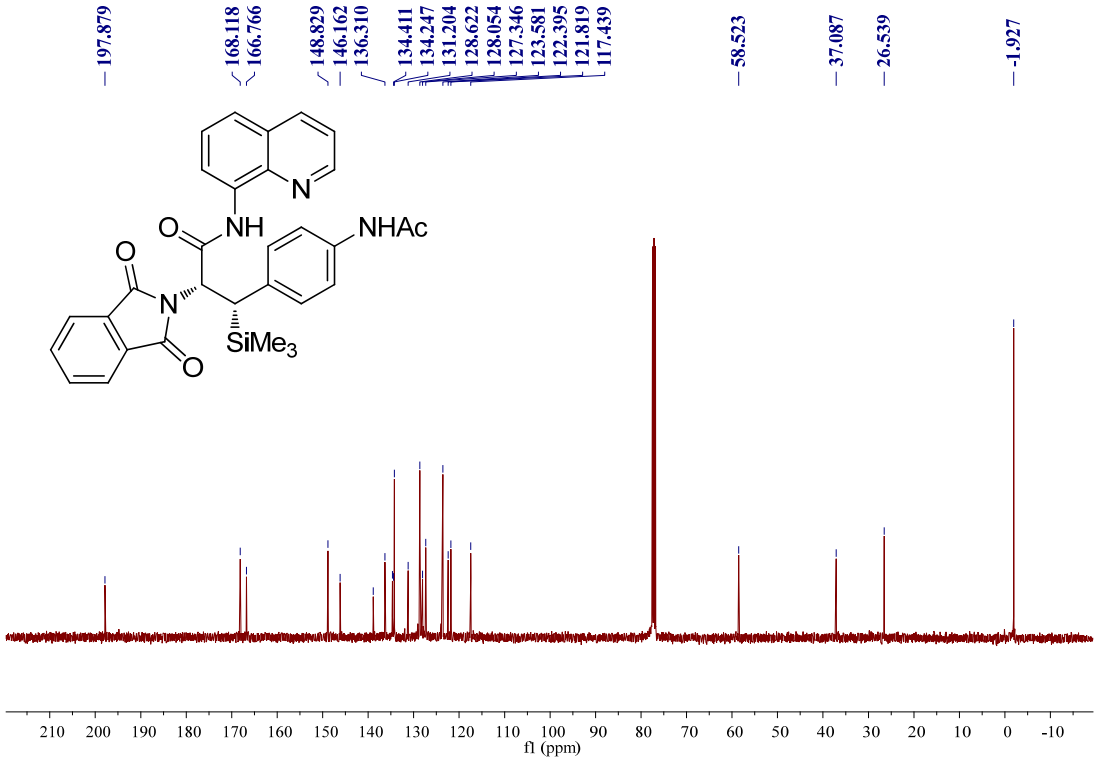

168.262
167.316
148.808
136.266
134.043
131.368
128.367
128.066
127.365
125.538
123.411
122.262
121.763
117.458
59.319
36.534
-1.880
f1 (ppm)

3b

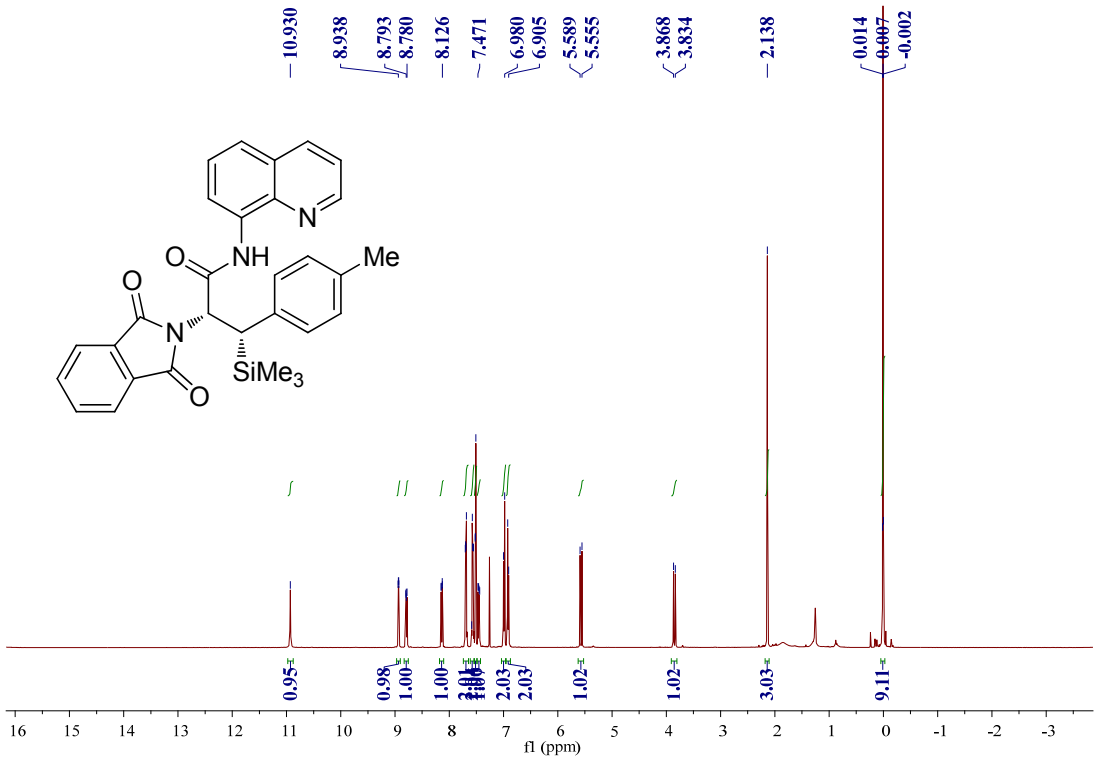

10.926
8.939
8.932
8.800
8.789
8.778
8.154
8.136
7.465
7.011
6.681
6.660
5.551
5.517
3.837
3.804
3.656
0.009
N
O
NH
OMe
O
N
SiMe3
O
0.92
0.95
1.00
1.00
2.01
2.01
1.00
1.03
3.03
9.06
12.5 11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
168.319
167.424
157.410
148.813
136.273
134.636
134.070
131.528
131.432
128.079
127.379
123.461
122.250
121.762
117.479
113.848
59.545
55.182
35.410
-1.877
N
O
NH
OMe
O
N
SiMe3
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

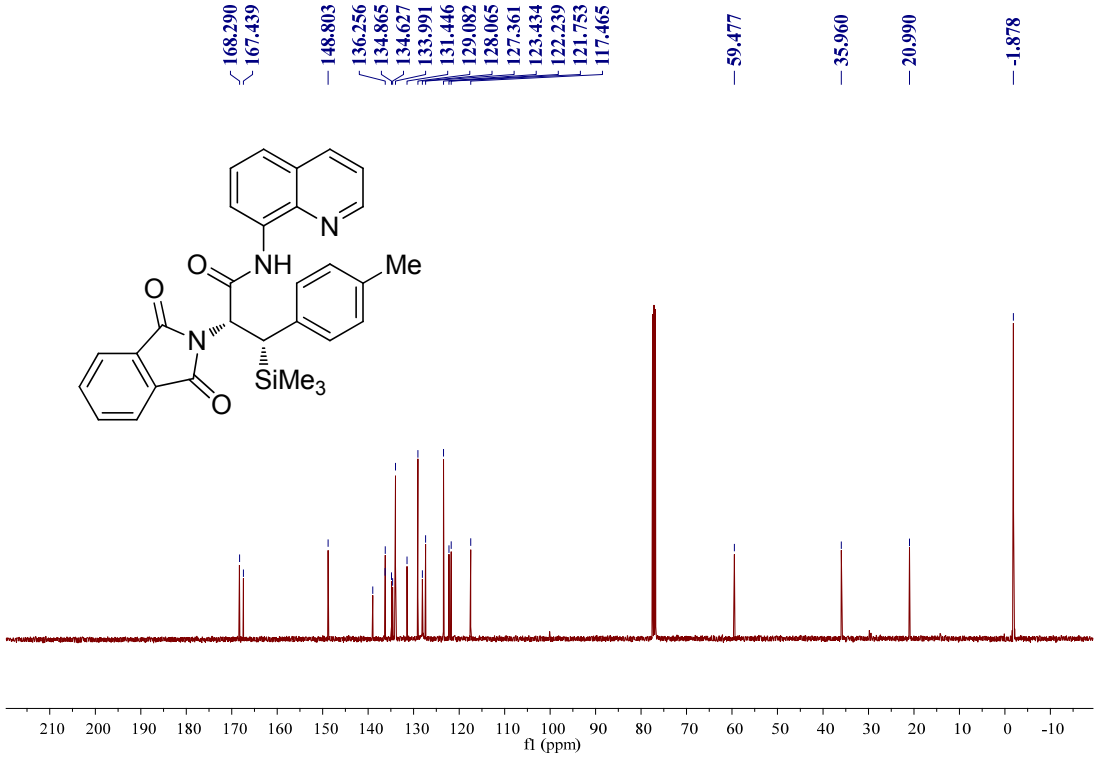
3c


10.847
8.910
8.785
8.763
7.705
7.674
7.571
7.465
7.200
5.651
5.617
4.076
4.043
2.469
0.028
NH
NHAc
SiMe3
0.99
1.02
1.01
2.06
1.98
1.95
1.07
2.02
1.00
1.06
3.07
9.12
fl (ppm)

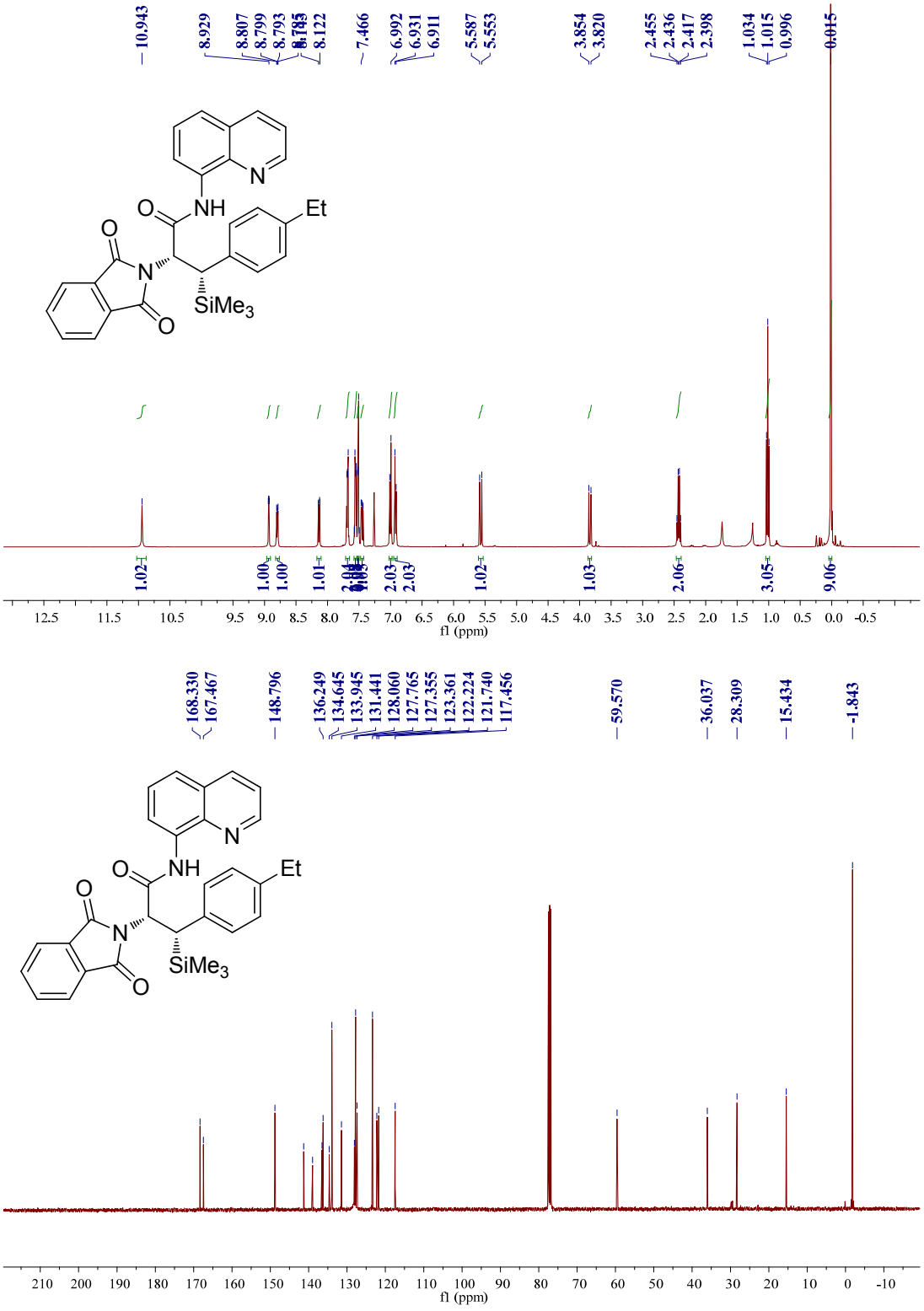

197.879
168.118
166.766
148.829
146.162
136.310
134.411
134.247
131.204
128.622
128.054
127.346
123.581
122.395
121.819
117.439
58.523
37.087
26.539
-1.927
NH
NHAc
SiMe3
fl (ppm)

3d

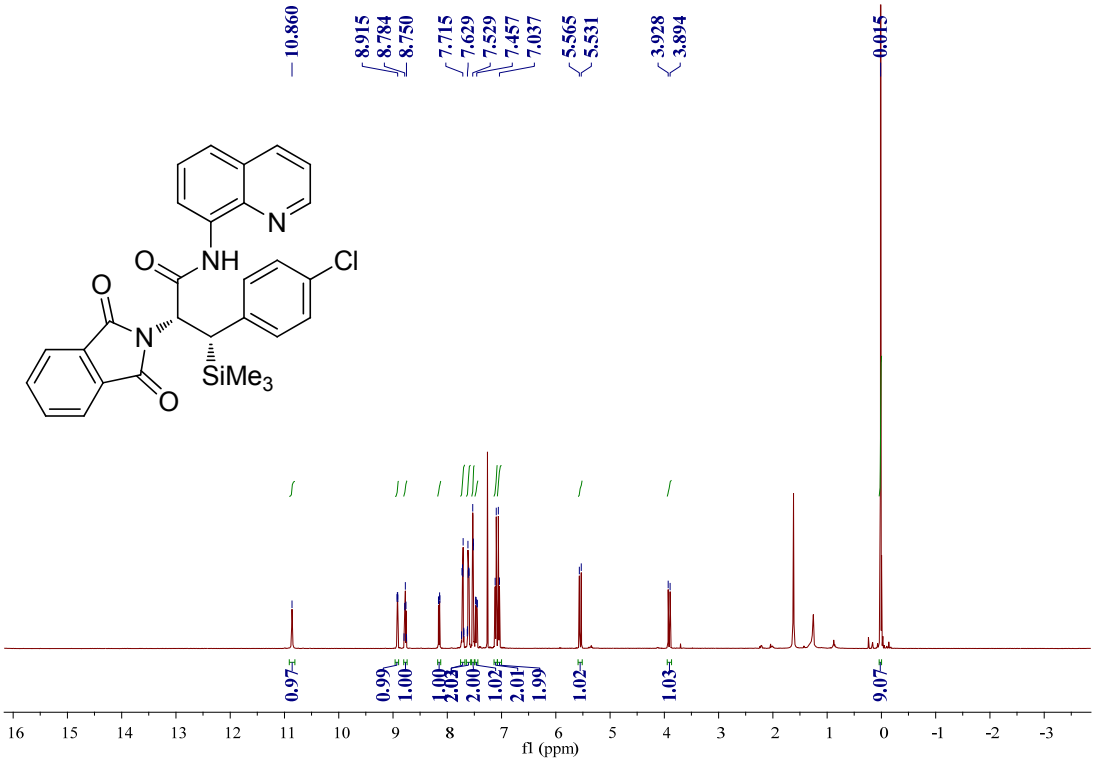

10.930
8.938
8.793
8.780
8.126
7.471
6.980
6.905
5.589
5.555
3.868
3.834
2.138
0.014
0.007
-0.002
N
NH
O
Me
O
N
O
SiMe3
0.95
0.98
1.00
1.00
2.03
2.03
1.02
1.02
3.03
9.11
f1 (ppm)

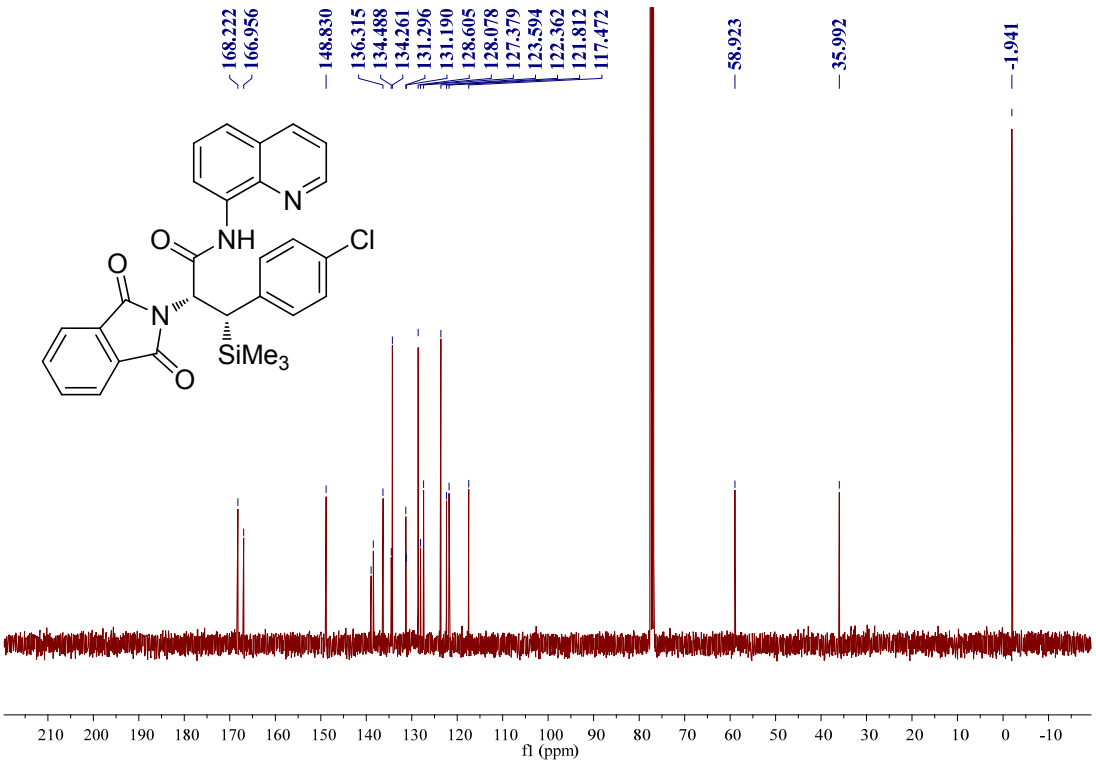

168.290
167.439
148.803
136.256
134.865
134.627
133.991
131.446
129.082
128.065
127.361
123.434
122.239
121.753
117.465
59.477
35.960
20.990
-1.878
N
NH
O
Me
O
N
O
SiMe3
f1 (ppm)

3e

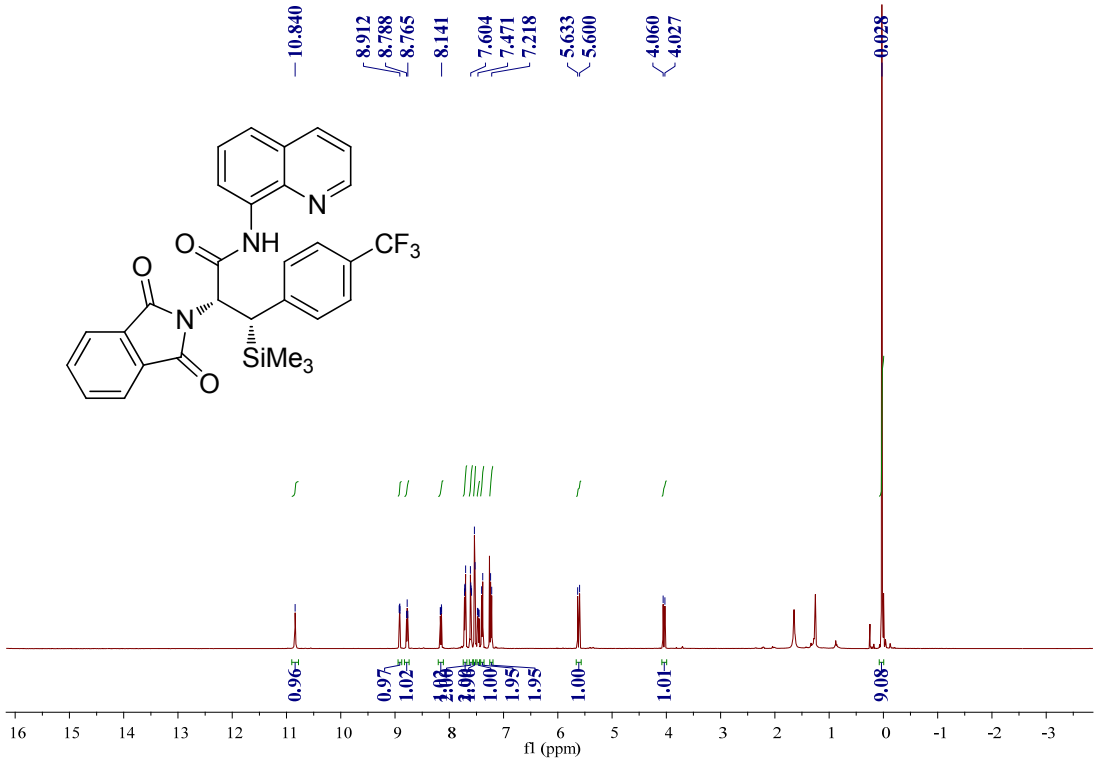

10.943
8.929
8.807
8.799
8.793
8.122
7.466
6.992
6.931
6.911
5.587
5.553
3.854
3.820
2.455
2.436
2.417
2.398
1.034
1.015
0.996
0.015
N
NH
O
Et
O
N
SiMe3
O
1.02
1.00
1.00
1.01
2.03
2.03
1.02
1.03
2.06
3.05
9.06
f1 (ppm)
168.330
167.467
148.796
136.249
134.645
133.945
131.441
128.060
127.765
127.355
123.361
122.224
121.740
117.456
59.570
36.037
28.309
15.434
-1.843
f1 (ppm)

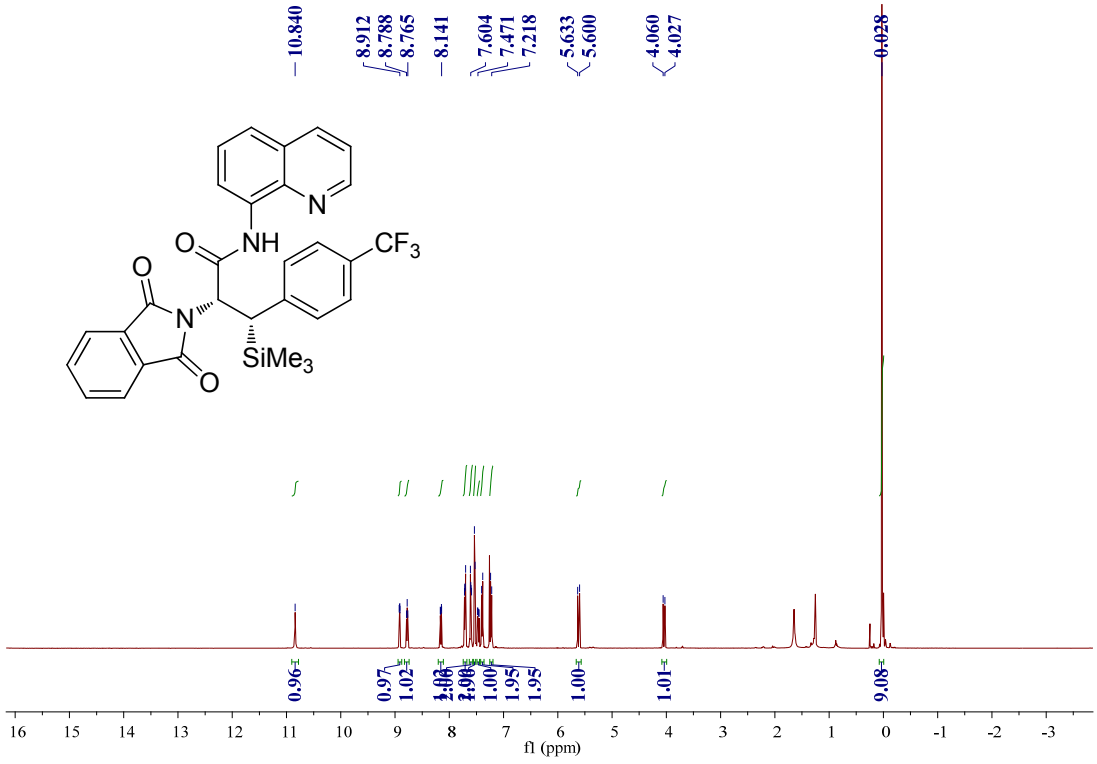
3f


10.860
8.915
8.784
8.750
7.715
7.629
7.529
7.457
7.037
5.565
5.531
3.928
3.894
0.015
0.97
0.99
1.00
1.00
2.03
2.00
1.02
2.01
1.99
1.02
1.03
9.07
fl (ppm)

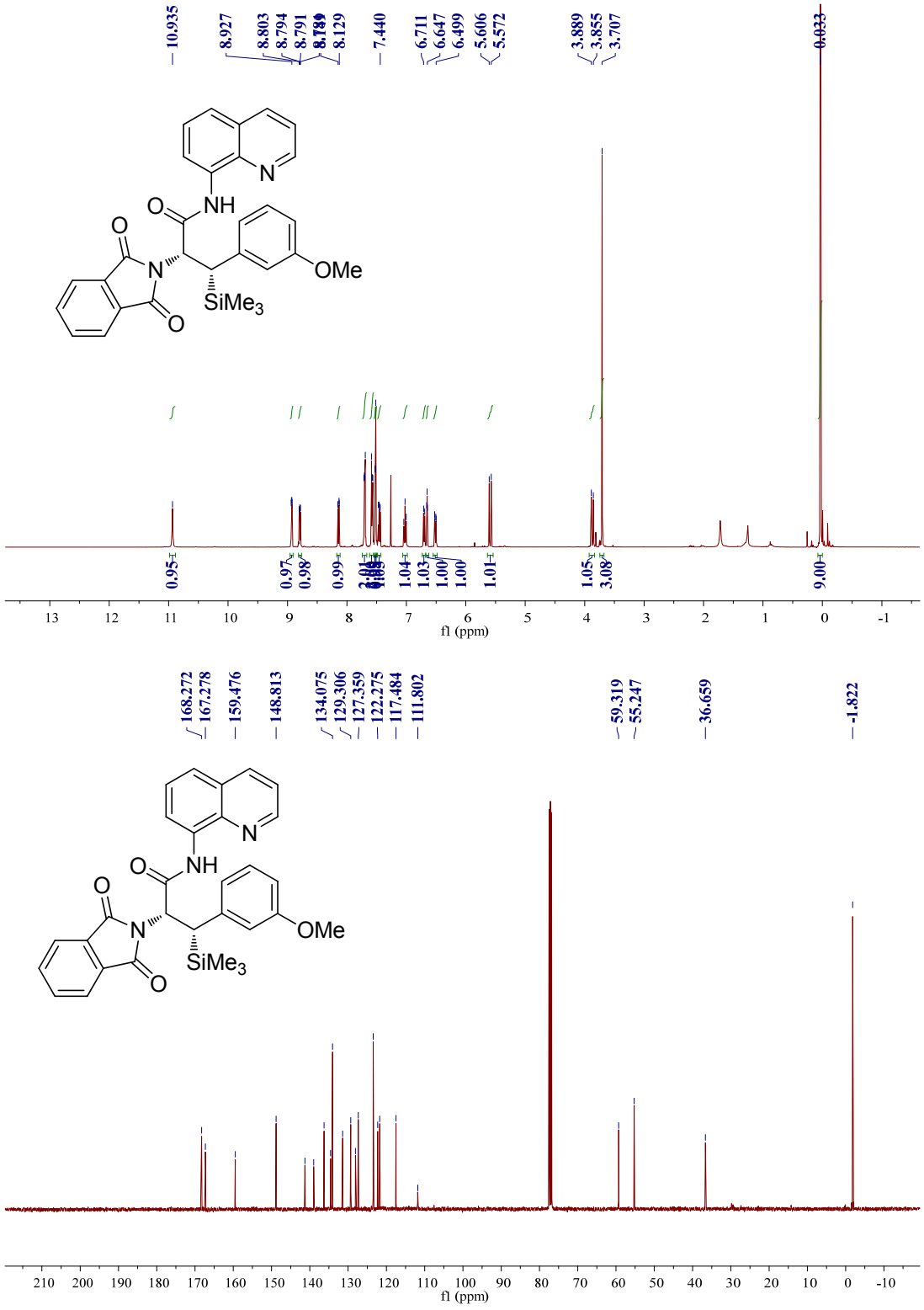

168.222
166.956
148.830
136.315
134.488
134.261
131.296
131.190
128.605
128.078
127.379
123.594
122.362
121.812
117.472
58.923
35.992
-1.941
fl (ppm)

3g

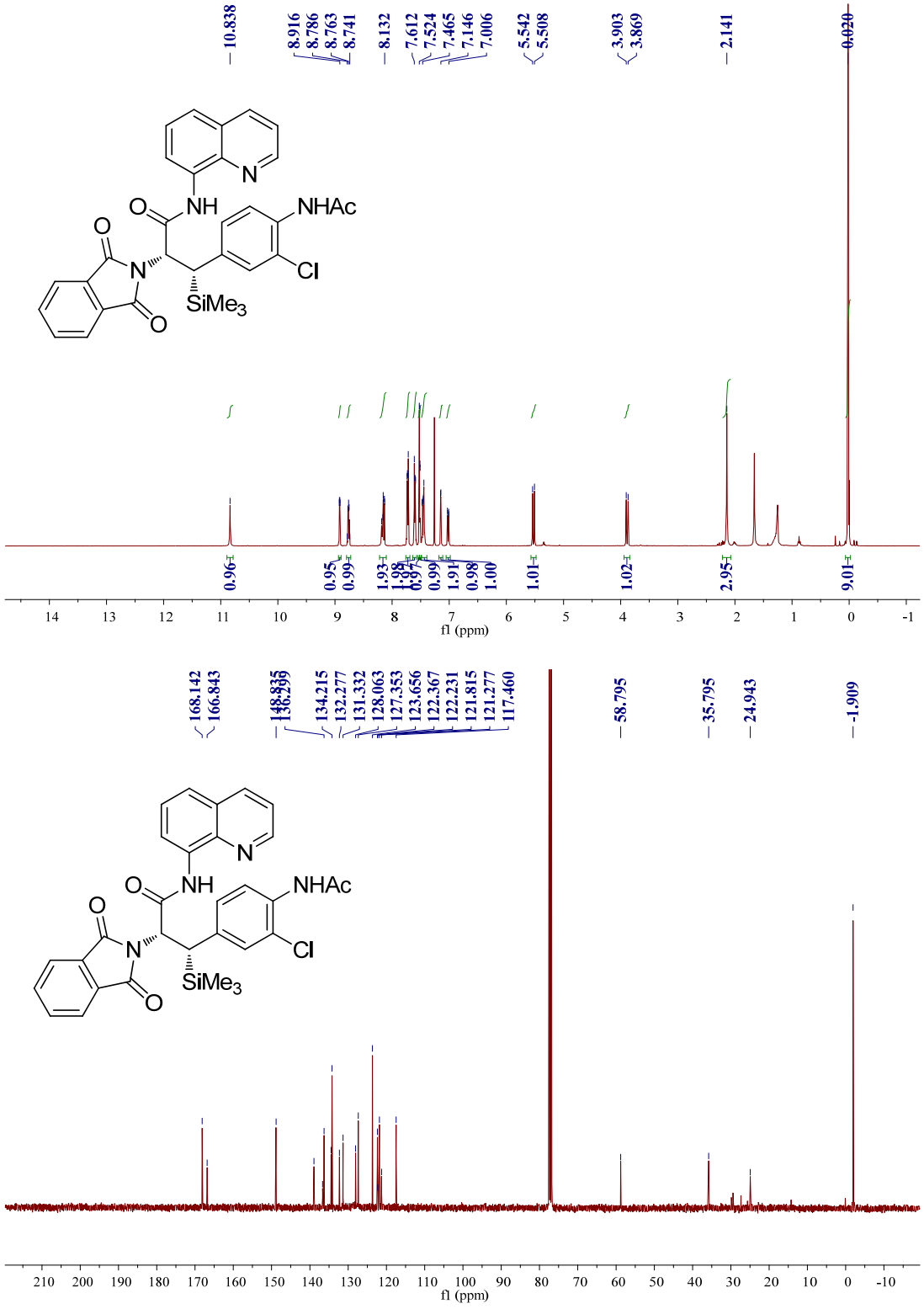

10.840
8.912
8.788
8.765
8.141
7.604
7.471
7.218
5.633
5.600
4.060
4.027
0.028
0.96
0.97
1.02
1.00
1.00
1.95
1.95
1.00
1.01
9.08
f1 (ppm)


10.840
8.912
8.788
8.765
8.141
7.604
7.471
7.218
5.633
5.600
4.060
4.027
0.028
0.96
0.97
1.02
1.00
1.00
1.95
1.95
1.00
1.01
9.08
f1 (ppm)

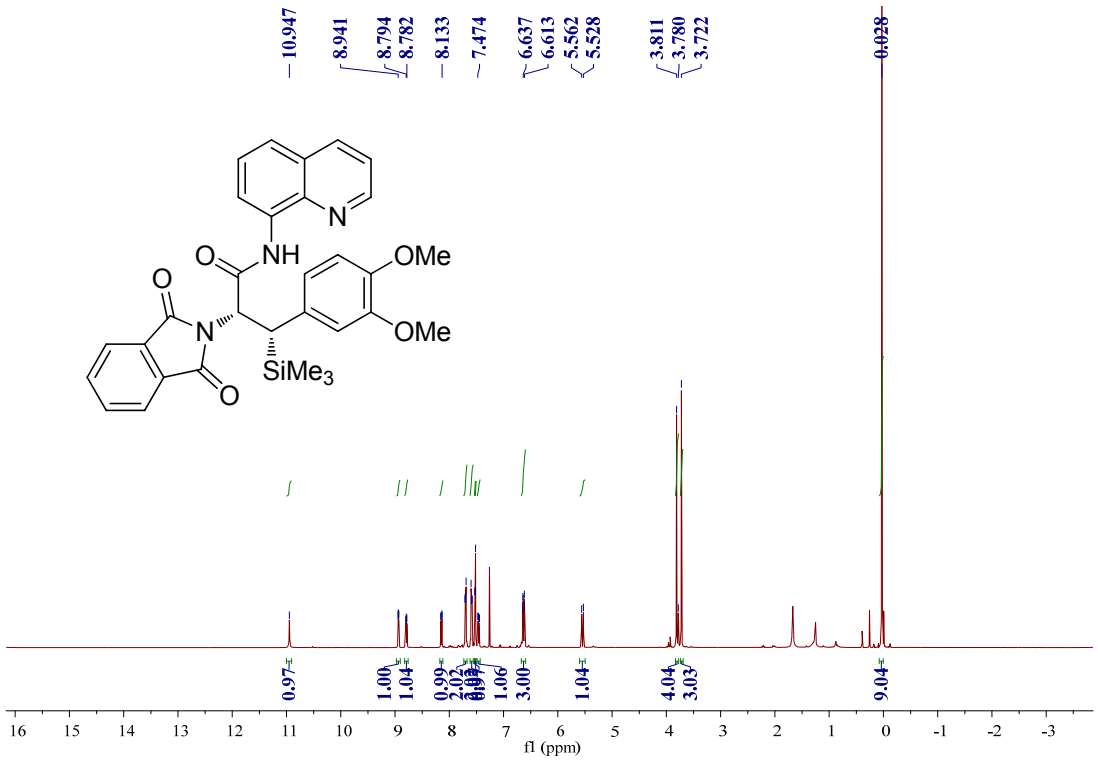
3h

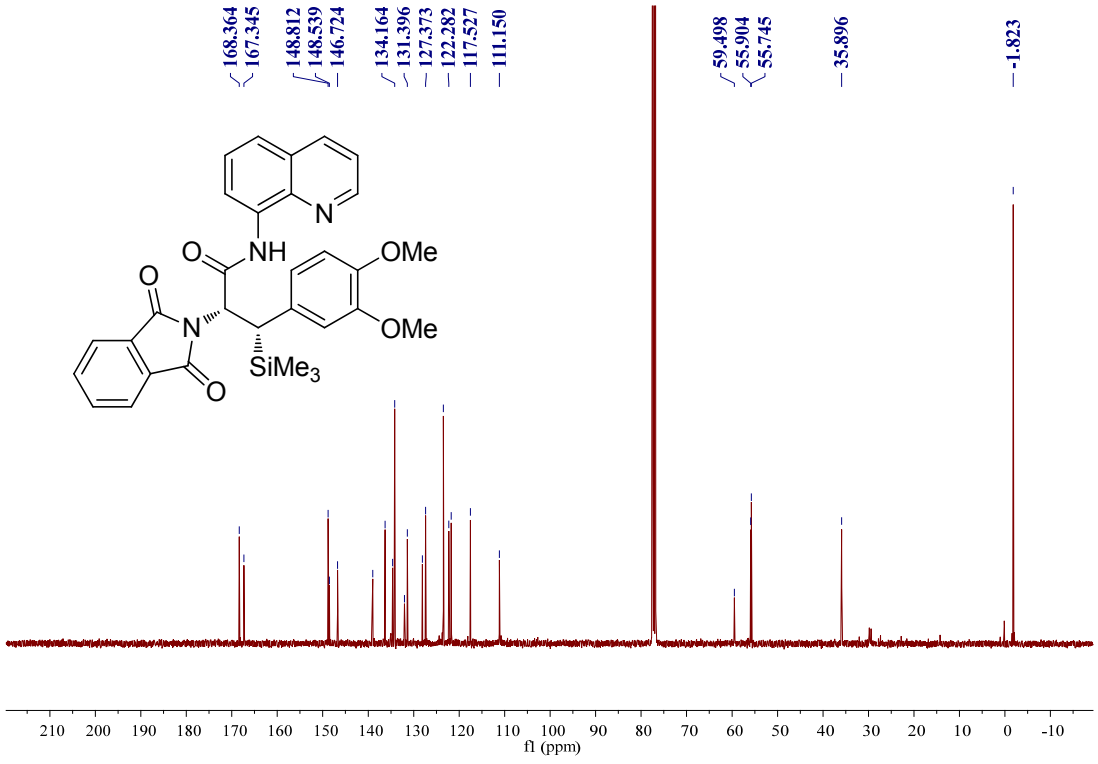

10.935
8.927
8.803
8.794
8.791
8.129
7.440
6.711
6.647
6.499
5.606
5.572
3.889
3.855
3.707
0.033
0.95
0.97
0.98
0.99
1.04
1.03
1.00
1.00
1.01
1.05
3.08
9.00
f1 (ppm)
168.272
167.278
159.476
148.813
134.075
129.306
127.359
122.275
117.484
111.802
59.319
55.247
36.659
-1.822
f1 (ppm)

3i

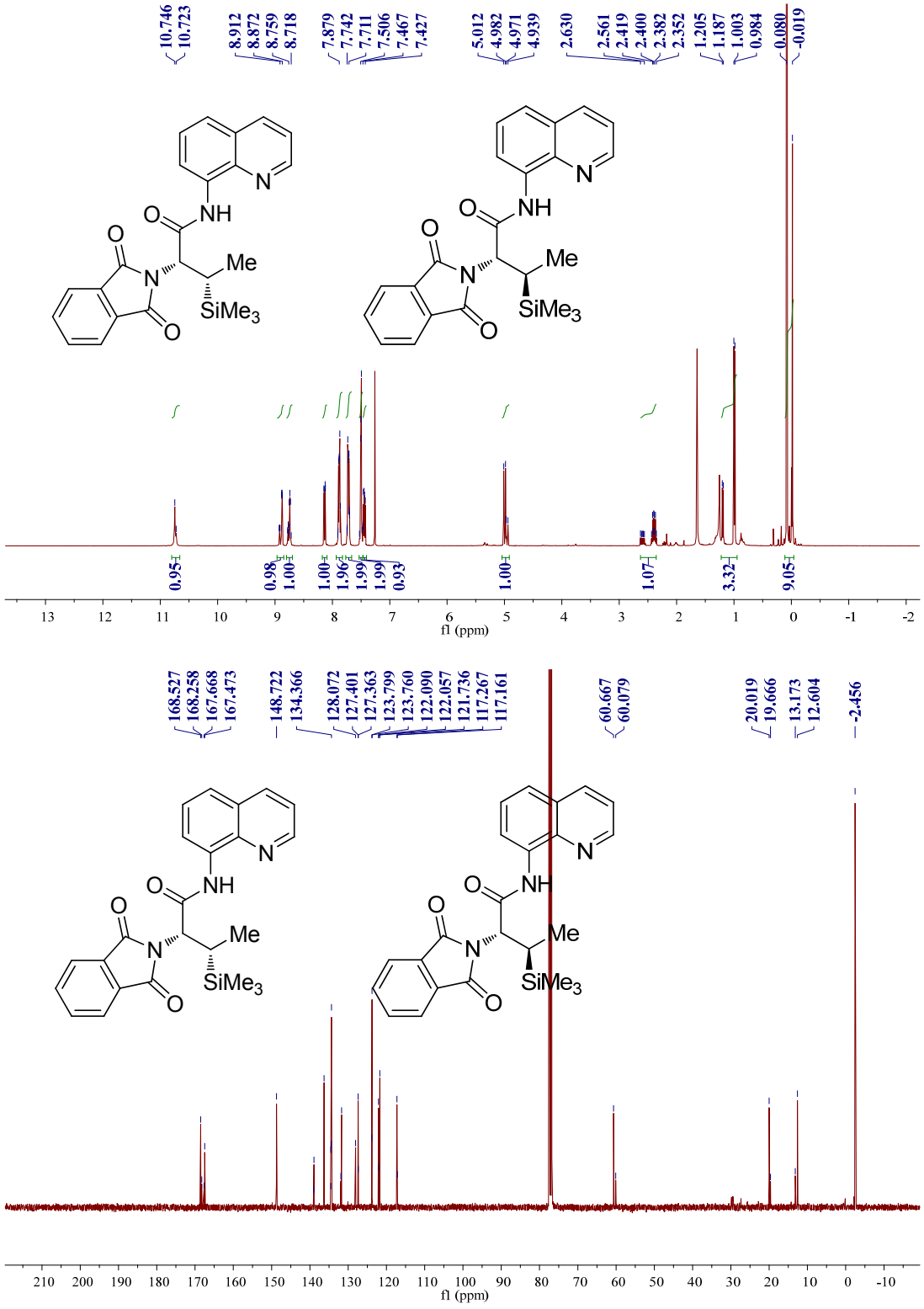

10.838
8.916
8.786
8.763
8.741
8.132
7.612
7.524
7.465
7.146
7.006
5.542
5.508
3.903
3.869
2.141
0.020
NH
NHAc
Cl
SiMe3
0.96
0.95
0.99
1.93
1.98
0.97
0.99
1.91
0.98
1.00
1.01
1.02
2.95
9.01
f1 (ppm)
168.142
166.843
148.835
138.296
134.215
132.277
131.332
128.063
127.353
123.656
122.367
122.231
121.815
121.277
117.460
58.795
35.795
24.943
-1.909
f1 (ppm)

3j

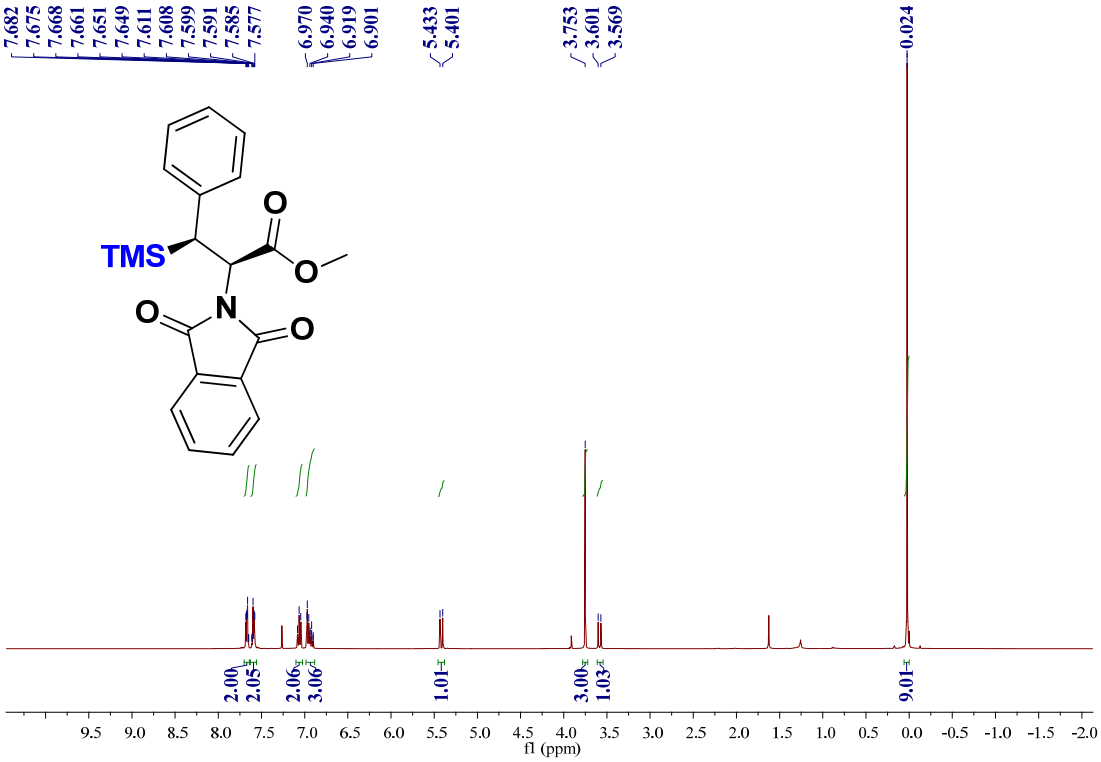

10.947
8.941
8.794
8.782
8.133
7.474
6.637
6.613
5.562
5.528
3.811
3.780
3.722
0.028
0.97
1.00
1.04
0.99
1.06
3.00
1.04
4.04
3.03
9.04
f1 (ppm)

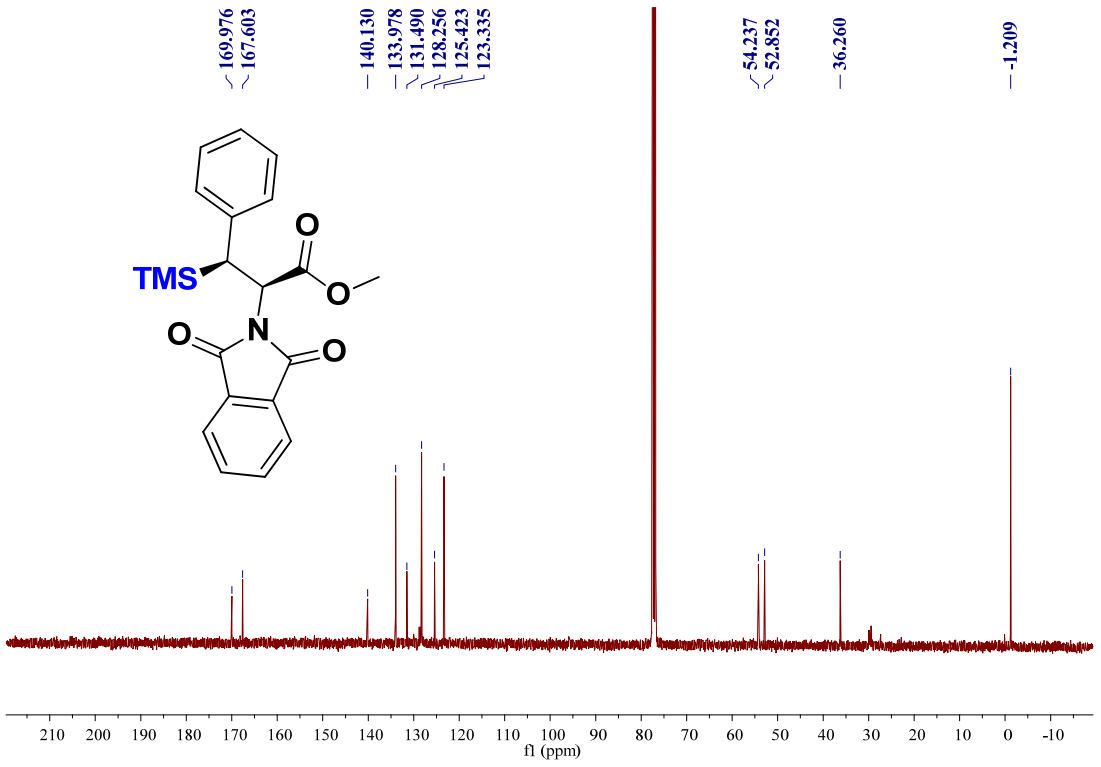

168.364
167.345
148.812
148.539
146.724
134.164
131.396
127.373
122.282
117.527
111.150
59.498
55.904
55.745
35.896
-1.823
f1 (ppm)

3k

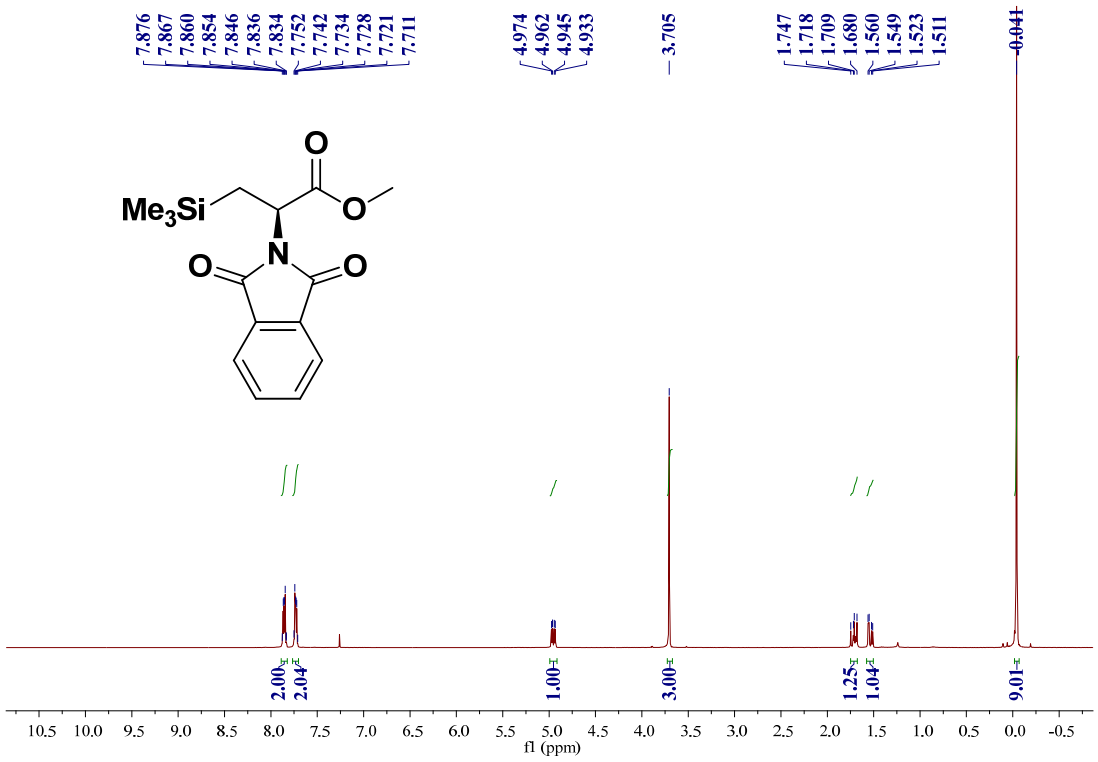

10.746
10.723
8.912
8.872
8.759
8.718
7.879
7.742
7.711
7.506
7.467
7.427
5.012
4.982
4.971
4.939
2.630
2.561
2.419
2.400
2.382
2.352
1.205
1.187
1.003
0.984
0.080
-0.019
0.95
0.98
1.00
1.00
1.96
1.99
1.99
0.93
1.00
1.07
3.32
9.05
f1 (ppm)
168.527
168.258
167.668
167.473
148.722
134.366
128.072
127.401
127.363
123.799
123.760
122.090
122.057
121.736
117.267
117.161
60.667
60.079
20.019
19.666
13.173
12.604
-2.456
f1 (ppm)

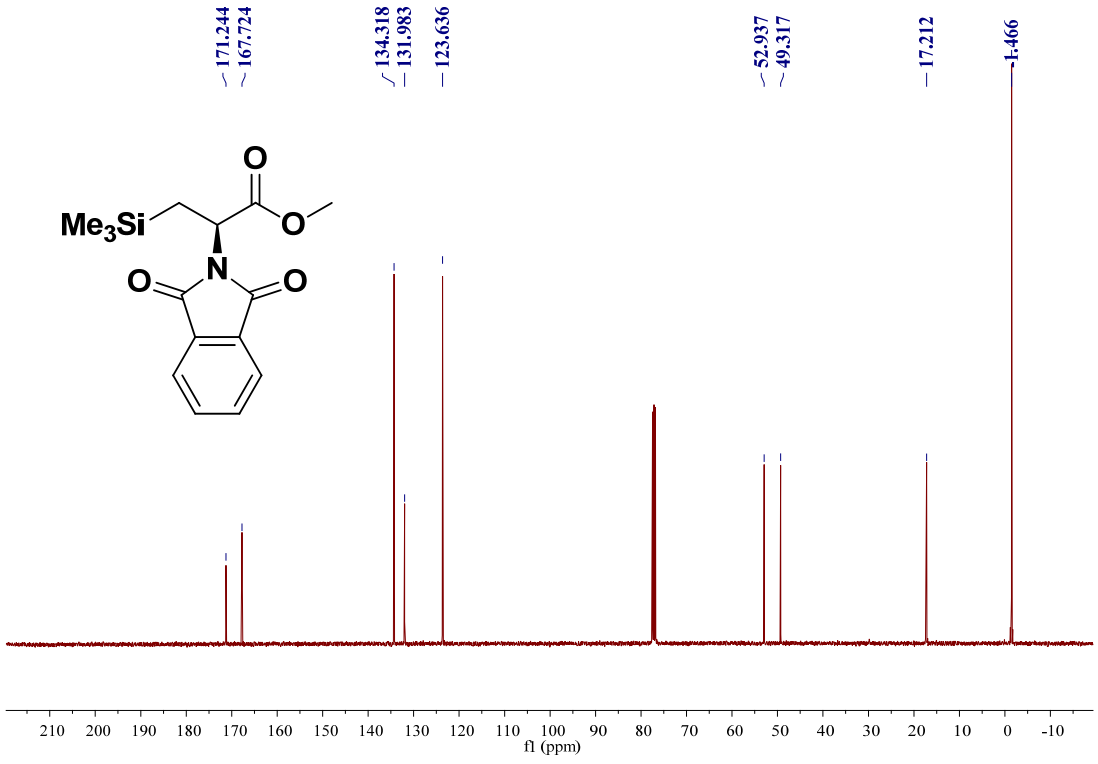
4a


7.682
7.675
7.668
7.661
7.651
7.649
7.611
7.608
7.599
7.591
7.585
7.577
6.970
6.940
6.919
6.901
5.433
5.401
3.753
3.601
3.569
0.024
TMS
O
O
N
O
O
2.00
2.05
2.06
3.06
1.01
3.00
1.03
9.01
f1 (ppm)

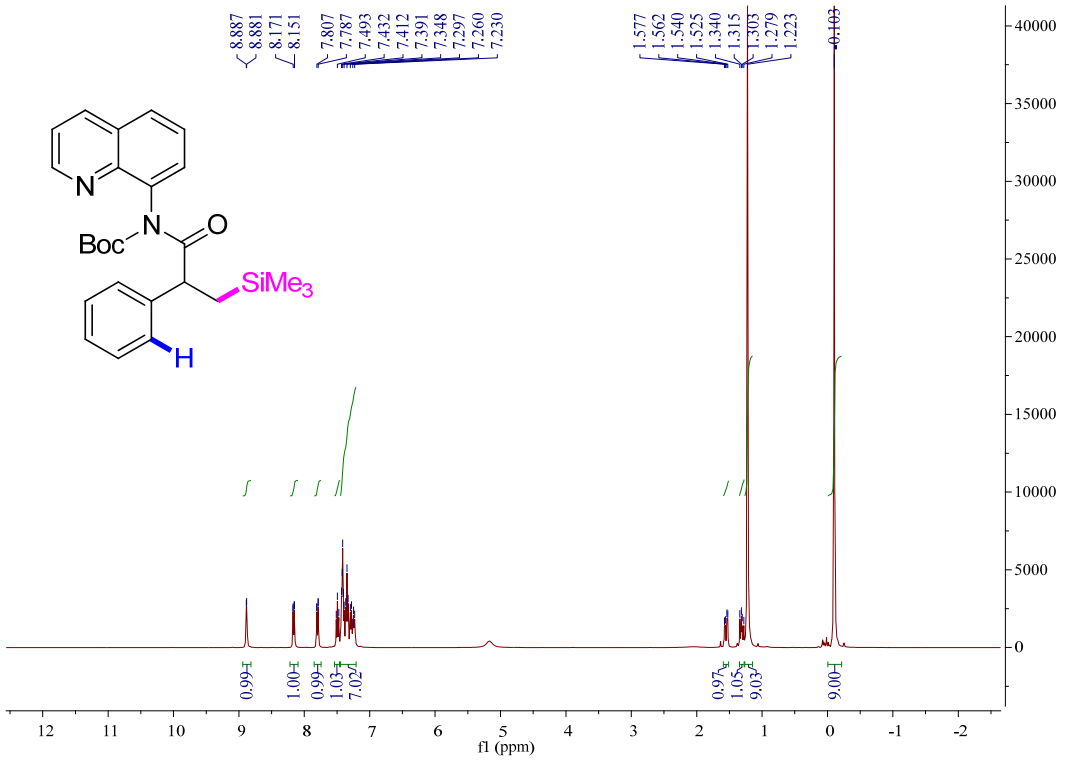

169.976
167.603
140.130
133.978
131.490
128.256
125.423
123.335
54.237
52.852
36.260
-1.209
TMS
O
O
N
O
O
f1 (ppm)

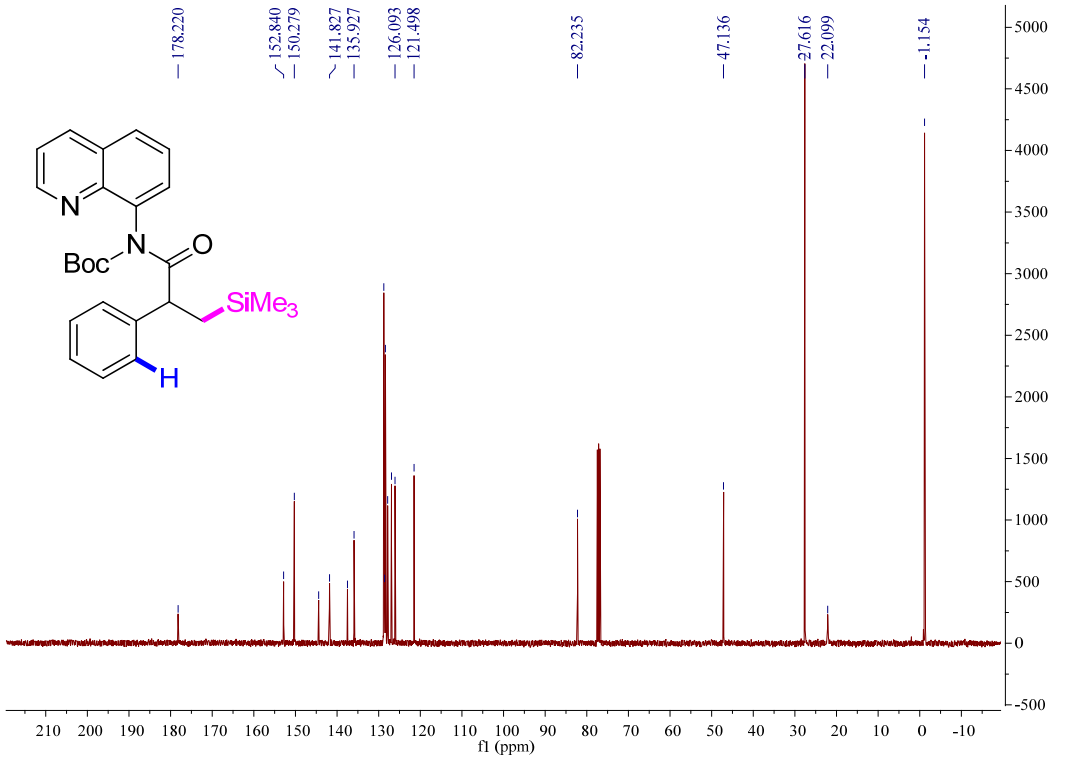
1aa


7.876
7.867
7.860
7.854
7.846
7.836
7.834
7.752
7.742
7.734
7.728
7.721
7.711
4.974
4.962
4.945
4.933
3.705
1.747
1.718
1.709
1.680
1.560
1.549
1.523
1.511
0.041
Me3Si
O
N
2.00
2.04
1.00
3.00
1.25
1.04
9.01
f1 (ppm)

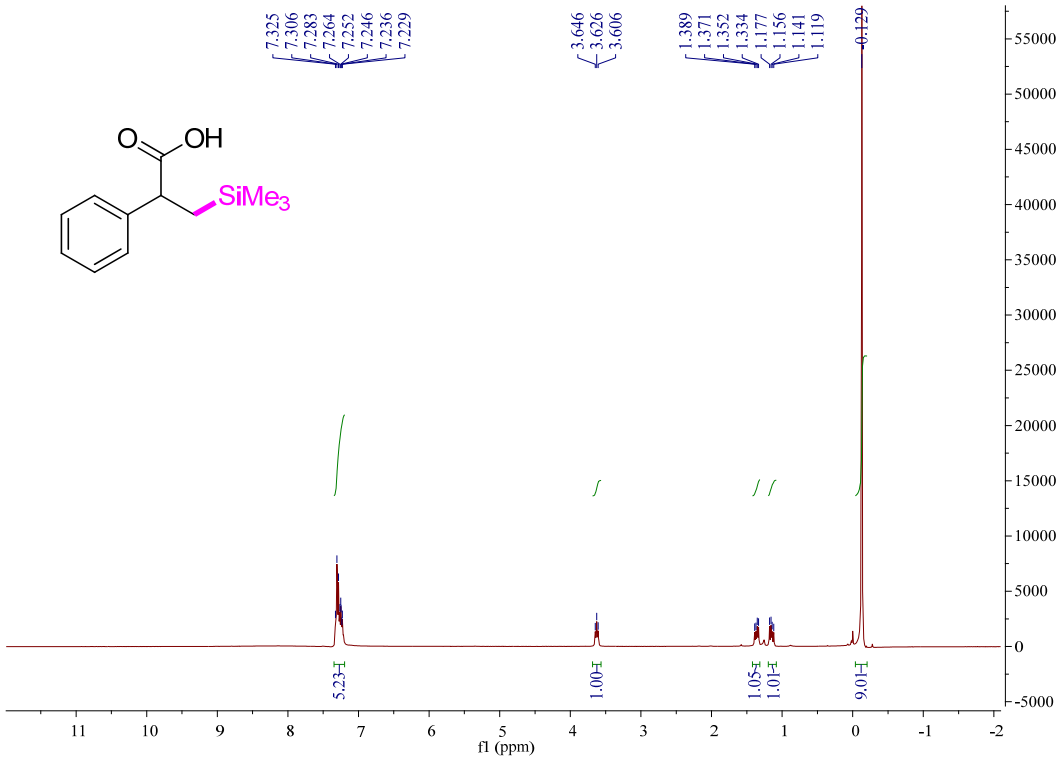

171.244
167.724
134.318
131.983
123.636
52.937
49.317
17.212
1.466
Me3Si
O
N
f1 (ppm)

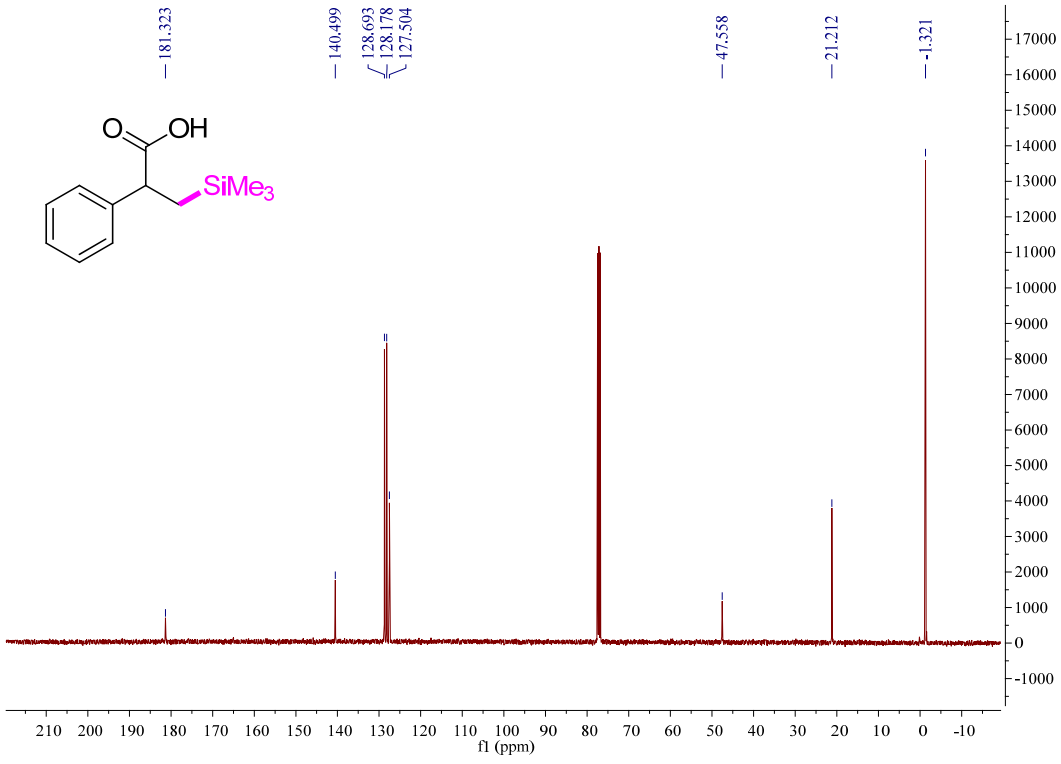
7


8.887
8.881
8.171
8.151
7.807
7.787
7.493
7.432
7.412
7.391
7.348
7.297
7.260
7.230
1.577
1.562
1.540
1.525
1.340
1.315
1.303
1.279
1.223
0.103
N
Boc
N
O
SiMe3
H
0.99
1.00
0.99
1.03
7.02
0.97
1.05
9.03
9.00
f1 (ppm)

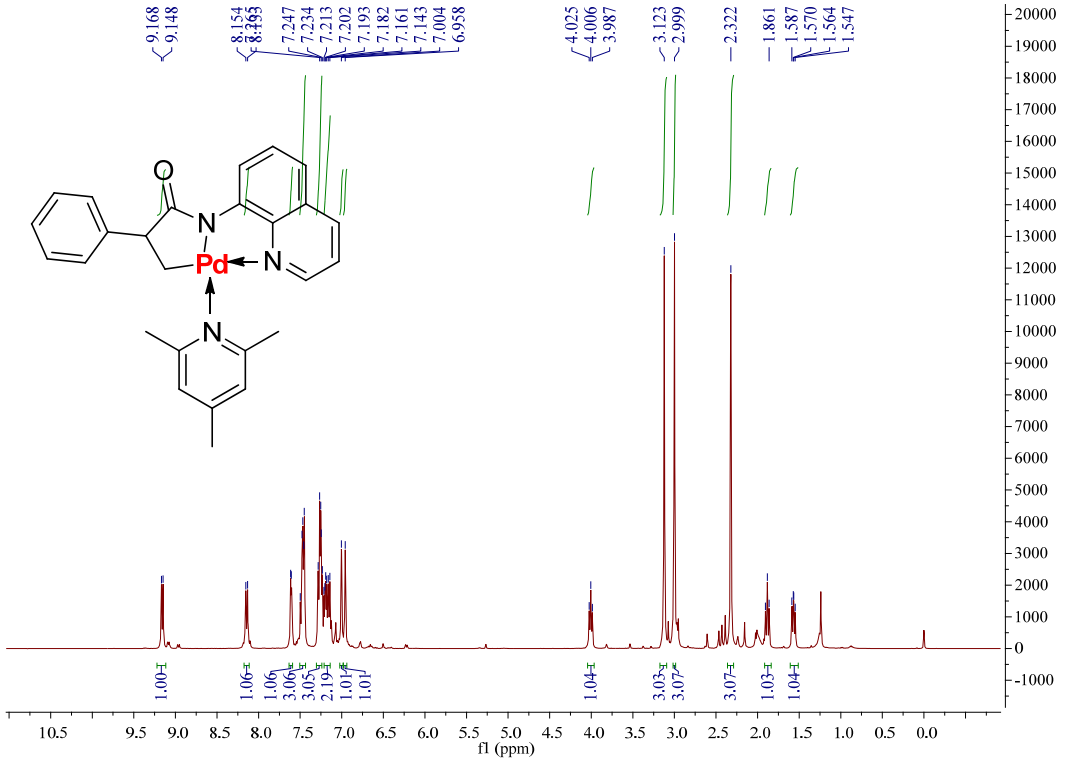

178.220
152.840
150.279
141.827
135.927
126.093
121.498
82.235
47.136
27.616
22.099
-1.154
N
Boc
N
O
SiMe3
H
f1 (ppm)

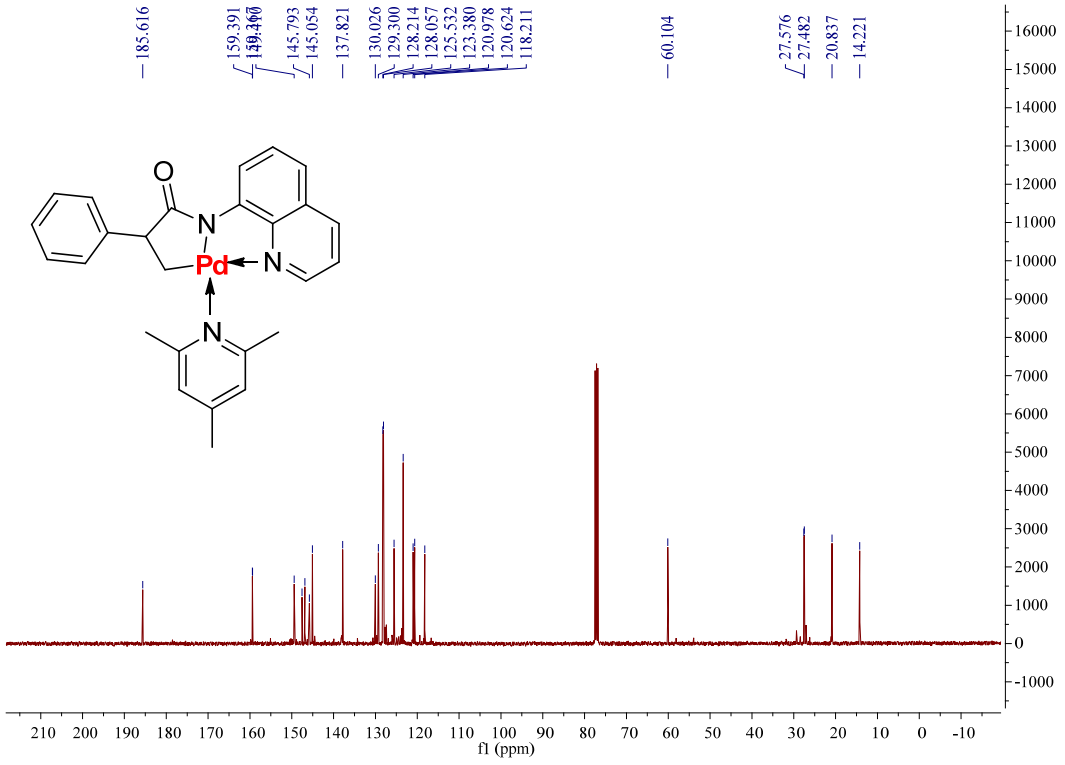
6aa


7.325
7.306
7.283
7.264
7.252
7.246
7.236
7.229
3.646
3.626
3.606
1.389
1.371
1.352
1.334
1.177
1.156
1.141
1.119
0.129
O
OH
SiMe3
5.23
1.00
1.05
1.01
9.01
f1 (ppm)

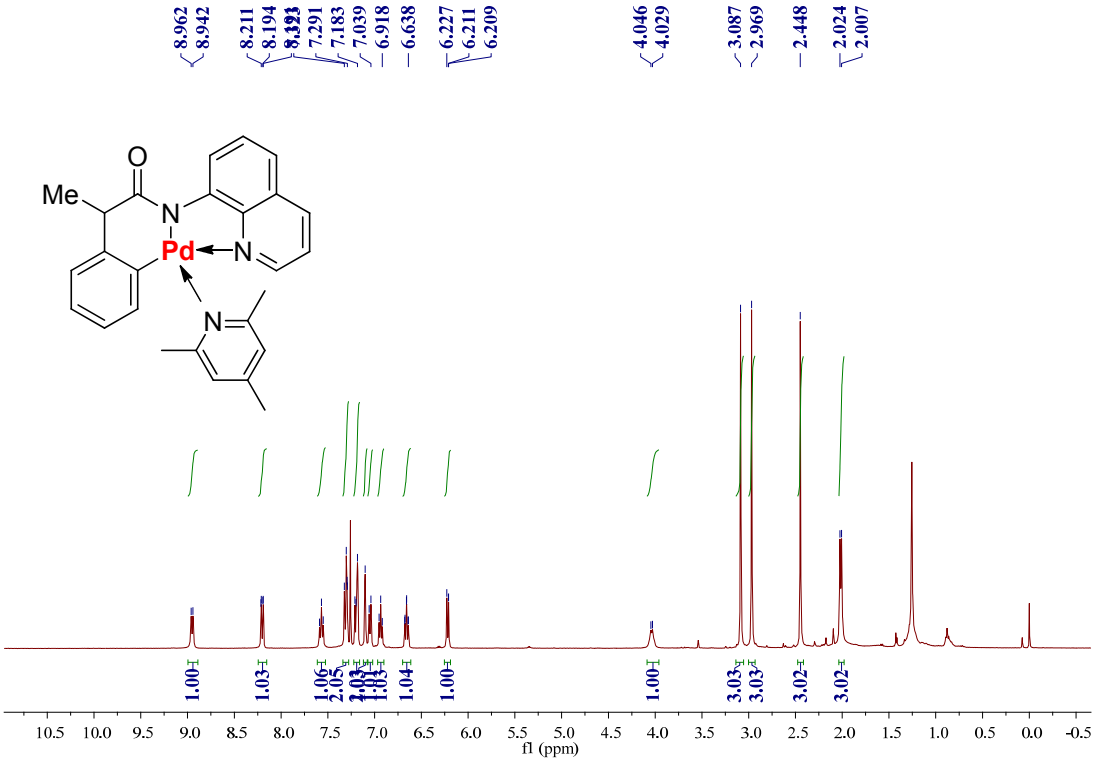

181.323
140.499
128.693
128.178
127.504
47.558
21.212
-1.321
O
OH
SiMe3
f1 (ppm)

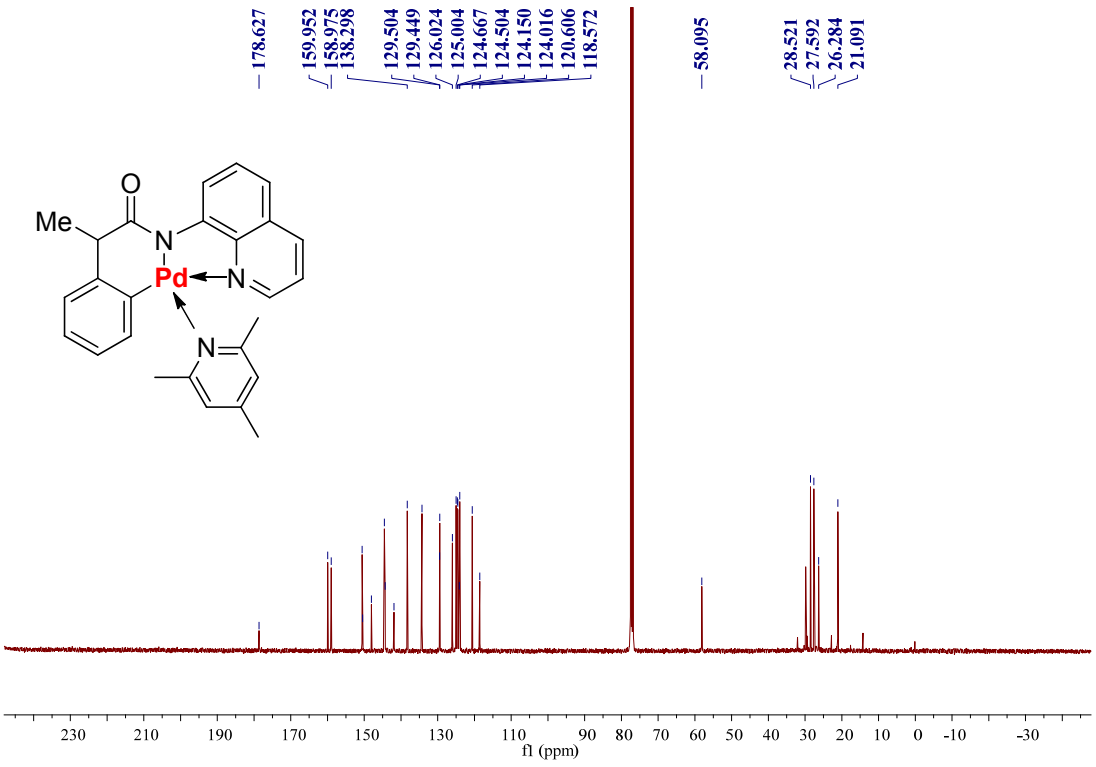
Int-C


9.168
9.148
8.154
7.247
7.234
7.213
7.202
7.193
7.182
7.161
7.143
7.004
6.958
4.025
4.006
3.987
3.123
2.999
2.322
1.861
1.587
1.570
1.564
1.547
O
N
Pd
N
N
1.00
1.06
1.06
3.06
3.05
2.19
1.01
1.01
1.04
3.03
3.07
3.07
1.03
1.04
f1 (ppm)


185.616
159.391
145.793
145.054
137.821
130.026
129.300
128.214
128.057
125.532
123.380
120.978
120.624
118.211
60.104
27.576
27.482
20.837
14.221
O
N
Pd
N
N
f1 (ppm)

Int-D


8.962
8.942
8.211
8.194
7.291
7.183
7.039
6.918
6.638
6.227
6.211
6.209
4.046
4.029
3.087
2.969
2.448
2.024
2.007
Me
O
N
Pd
N
N
1.00
1.03
1.06
2.05
1.04
1.00
1.00
3.03
3.03
3.02
3.02
f1 (ppm)


178.627
159.952
158.975
138.298
129.504
129.449
126.024
125.004
124.667
124.504
124.150
124.016
120.606
118.572
58.095
28.521
27.592
26.284
21.091
Me
O
N
Pd
N
N
f1 (ppm)